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HISTOPATHOLOGY OF POLIOENCEPHALITIS HEMORRHAGICA SUPERIOR (WERNICKE'S DISEASE)

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THE CONDITION named polioencephalitis hemorrhagica superior by Wernicke [1] was considered by him to be largely, yet not entirely, due to alcohol poisoning. The symptoms are palsies of the ocular muscles, which finally lead to complete paralysis, reeling gait, vertigo, headache, nystagmus, optic neuritis, photophobia and disturbances of consciousness. The last-mentioned symptom may be characterized by drowsiness either from the onset or as a terminal state. External ophthalmoplegia may occur in varying degrees and combinations. Certain ocular muscles, such as the sphincter of the iris and the levator palpebrae, are usually unaffected. The pathologic process involves the origin of the upper cranial nerves but may extend to include the lower ones (polioencephalitis superior and inferior), resulting in bulbar paralysis. The disease follows an acute or a subacute course and usually ends in death in eight to fourteen days, but a more protracted course with ultimate recovery may occur. All 3 of Wernicke's original cases ended in death within a period of two weeks.

THEORIES OF CAUSE

The mechanism by which the chronic damage to the nervous system by alcoholism in this disease comes about is no longer considered to be directly traceable to the alcohol itself.[2] Alcohol is not the unique cause, and its action in some instances may be secondary; yet the fact remains that the clinical and pathologic changes in this condition accompany not a few cases of chronic alcoholism. The trend of the explanation of the mechanism is away from the older assumption of a direct toxic action on nerve tissue of alcohol itself and, rather, toward

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1. Wernicke, C.: Lehrbuch der Gehirnkrankheiten, Berlin, T. Fischer, 1881, vol. 2, p. 229.

2. Alexander, L.: Neuropathology of Alcoholism, J. Nerv. & Ment. Dis. **90**: 385, 1939. Campbell, A. C. P., and Russell, W. R.: Wernicke's Encephalopathy (Polioencephalitis Hemorrhagica Superior): Its Alcoholic and Nonalcoholic Incidence, J. Path. & Bact. **48**:245, 1939.

a nutritional deficiency due to metabolic disturbances produced by the chronic ingestion of alcohol. These disturbances are due to neglect of proper diet by the chronically alcoholic person; incomplete absorption of vitamins from food due to gastritis and intestinal changes produced by alcoholism, and a condition of increased vitamin requirement due to the high caloric effect of alcohol.

NATURE OF THE PROBLEM

The purpose of this investigation was to determine the pathologic changes resulting from the metabolic disturbances produced by chronic alcoholic toxicosis, which develops after five to forty-five years of excessive alcoholism. There are two chronic clinical conditions, namely, alcoholic polyneuritis and alcoholic psychosis, each of which has its own characteristic lesions.

The pathologic process in polyneuritis is characterized by central and peripheral neuronitis, with swelling of ganglion cells predominantly in the motor and frontal cortex and the anterior horns of the spinal cord, followed by degeneration of the nerve fibers, particularly of the myelin sheaths, in the peripheral and central nervous system. This condition has been produced in animals by depriving them of thiamine and resembles the clinical condition of beriberi or pellagra.

The pathologic changes in alcoholic psychosis are characterized by small foci of degeneration and varicose deformity of vessels, proliferation of blood vessels and increase of the fixed cells of the vessel walls, subacute necrosis of the parenchyma and proliferation of the glia, with or without ring hemorrhages. The changes occur predominantly in the basal portion of the diencephalon, midbrain and medulla and in the periaqueductal gray matter at the level of the oculomotor nuclei. These lesions were first described by Wernicke [1] as polioencephalitis hemorrhagica superior and inferior and later by Bumke and Kant.[3]

There are two phases of the structural change of the latter condition to which further study and consideration may be given. The first is its interpretation in terms of known biochemical reactions; the other concerns the changes in the nerve cells and in the connective tissue of the brain, namely, the neuroglial elements.

MATERIAL

The material used in this study consisted of central nervous tissue obtained from 5 cases, the specimens of which had accumulated in the Cajal laboratory of the Los Angeles General Hospital. In each case there were a history of chronic alcoholism and the clinical symptoms and findings of Wernicke's polioencephalitis hemorrhagica superior. The clinical history and gross pathologic changes in the brain in each case are presented.

3. Bumke, O., and Kant, E., in Bumke, O., and Forster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 13, p. 852.

CASE 1.—A white woman aged 52 had fainted three months previous to her admission and had not been clear mentally since that time. She was disoriented at times with regard to place and was said to have had convulsions on the day of entry to the hospital. The sister stated that the patient was chronically alcoholic. Her pupils were equal but not regular and reacted sluggishly to light and in accommodation. Her heart was regular and her lungs were clear. All reflexes were absent, and there was marked degeneration of the fundal vessels of the retina. Laboratory tests gave normal results. Two weeks after admission she died, with a temperature of 106.4 F., a pulse rate of 136 and a respiratory rate of 40 per minute.

Gross examination of the brain at autopsy showed that the convolutions of the central region were somewhat atrophied and the arachnoid somewhat thickened and opaque, indicating a slight chronic arachnoiditis with early cortical atrophy. Repeated sections of the whole brain showed no gross alterations and no areas of hemorrhage or necrosis.

CASE 2.—A white male laborer aged 50 was admitted to the hospital with swollen ankles, weakness and anorexia, which he had had for several weeks. For five months his diet had been impoverished, and he had consumed at least 2 quarts (2 liters) of muscatel wine daily. His blood pressure was 85 systolic and 70 diastolic. There were moist rales in both lungs. Both ankles showed pitting edema. The routine laboratory tests gave normal or negative results. The electrocardiogram showed evidence of myocardial damage. The patient died fourteen days after admission.

Examination of the brain showed gross cortical atrophy with widening of the sulci. The blood vessels were small, thin walled and hypoplastic.

CASE 3.—A white woman aged 46 entered the hospital with a history of chronic alcoholism and in a state of deep coma. Her pupils were irregular and unequal, the left being larger than the right. They were reactive to light. There was ptosis of both lids, more pronounced on the left. The left eyeball was fixed. Both optic disks were normal. There was slight weakness of the lower left side of the face. There was tremor of both hands and of the right leg. The extremities of the left side were weak. The deep reflexes were increased. The Babinski reflex was present bilaterally. The spinal fluid was slightly exanthochromic, and the Pandy reaction was 4 plus; a count showed 370 fresh red blood cells and 4 white blood cells per low power field. Her temperature ranged from 99.8 to 101.0 F., and she remained comatose. Twelve days after admission she died.

Gross examination of the brain showed no external markings. Repeated sections of the brain showed multiple small hemorrhages in the brain stem and periaqueductal region, with blood in the aqueduct. There were small hemorrhagic spots in the thalamus, the cerebral peduncles and the subthalamus and one in the medial nucleus of the right thalamus.

CASE 4.—A white man aged 69 entered the hospital with a history of chronic alcoholism and hemiplegia on the right side, which had developed during the past year. After his admission he became confused and incontinent. He was emaciated, and his tongue was red. He breathed rapidly and swallowed with difficulty. There were rales at the base of both lungs. His heart was enlarged to the left, and its rhythm was irregular, with extrasystoles. His blood pressure was 95 systolic and 60 diastolic, and his heart rate was 102. The only neurologic finding was a bilateral Babinski reflex. There were no pupillary changes. The laboratory tests all gave normal or negative results. Eight days later the patient became comatose; fibrillary twitching developed, and he died.

Examination of the brain showed grossly that the markings of the cortex were obliterated in both frontal poles, owing to edema of both frontal lobes.

CASE 5.—A white man aged 31 was in a slightly disoriented state on admission. He had been in fairly good health, except for occasional periods of drinking, until two weeks prior to admission, when anorexia and generalized malaise developed and lasted about two days. Then he had a generalized convulsion, which was followed by severe headache, sleepiness and a temperature as high as 102 F. Examination revealed that the patient was lethargic and acutely ill, with a temperature of 99.8 F., a pulse rate of 88, a respiration rate of 20 and a blood pressure of 124 systolic and 85 diastolic. The right pupil was slightly larger than the left, and the visual fields demonstrated bitemporal constriction. The Oppenheim and Kernig signs were elicited. The blood count and hemoglobin were normal. The spinal fluid was clear and under a pressure of 300 mm., and the cell count was 400 lymphocytes per cubic millimeter. The patient rapidly became worse and died on the third day after admission.

Examination of the brain showed grossly that the convolutions were slightly flattened and that there was a small amount of terminal subarachnoid hemorrhage of focal distribution, chiefly dorsolateral and frontal. There was also softening of the anterior third of the left temporal lobe. Sections of the hypothalamus showed continuation of this softening back to the insula and the lenticular nucleus. There was also hemorrhagic extravasation into the tegmental portions of the midbrain and fusiform hippocampal gyri of the same side.

The superficial changes in the brains in these cases were not consistent. However, within the brain stem of all 5 brains there was periaqueductal hemorrhage, which was apparent grossly in 2 of them. The cause of death in all 5 cases was polioencephalitis hemorrhagica superior.

BIOCHEMICAL FACTORS

The pathologic condition known as polioencephalitis hemorrhagica superior has been found associated with scurvy in nonalcoholic patients, as well as in alcoholic patients (Alexander and others [4]). In view of the fact that the ascorbic acid level in the blood plasma of patients with psychoses due to chronic alcoholism is consistently low, one might be led to the assumption that this disease is a cerebral form of scurvy. However, further experimental work by the previously mentioned investigators demonstrated that in pigeons the disease could be produced by thiamine deficiency, particularly if the birds were fed a sufficient supply of one or more other vitamins; namely, vitamin A, riboflavin, ascorbic acid and vitamin D, and that this disease could not be produced experimentally by a deficiency in ascorbic acid. However, deficiency in ascorbic acid may play a role in the predisposition to the disease. The conclusions reached by Alexander and associates [4] were as follows: The clinical symptoms of thiamine deficiency in the pigeon are specific

4. Alexander, L.; Pijoan, M.; Schube, P. G., and Moore, M.: Cevitamic Acid Content in Blood Plasma in Alcoholic Psychoses, Arch. Neurol. & Psychiat. **40**:58 (July) 1938.

for beriberi, e. g., ataxia, convulsions and local paresis; the total solids of the brain are decreased and the water content is correspondingly increased; the mineral skeleton of the nerve tissue, in contrast to similar conditions of other causes, remains unaltered and may be responsible for the reversibility of the process; the lesions of polioencephalitis hemorrhagica superior can be produced in pigeons lacking thiamine, especially if they receive other vitamin complexes, such as vitamin A, riboflavin, ascorbic acid and vitamin D; polioencephalitis hemorrhagica superior cannot be produced by deficiency of ascorbic acid, and the administration of vitamin A, riboflavin and vitamin D in cases of thiamine deficiency delays the onset of beriberi and prolongs the course of the disease once it is established.

Beriberi is characterized clinically by degenerative changes in the nervous system, including polyneuritis, which may exist alone but which is often accompanied by generalized edema and serous effusions and by a tendency to the development of cardiac hypertrophy, which frequently results in cardiac failure and sudden death.

HISTOPATHOLOGIC STUDY

The 5 brains which were studied in this investigation were fixed in solution of formaldehyde U. S. P. (1:4). The brain stem in each case was separated from the cerebral hemispheres, and transverse sections were cut through the midbrain, pons and medulla. Transverse sections from each of these brain stems were treated with the following staining procedures: hematoxylin and eosin, for the general histologic changes; the Cajal reduced silver method, for changes in neurons and neurofibrils; the Cajal gold chloride-mercury bichloride ("gold-sublimate") method, for changes in the astrocytes, and the Penfield combined method, for changes in the oligodendroglia and microglia.

General Histopathologic Changes. — Examination of microscopic sections of the brain stems stained with hematoxylin and eosin showed that the histopathologic changes in all 5 cases were confined largely, but not entirely, to the periventricular gray matter of the midbrain and the pons, i. e., throughout the hypothalamus, the mammillary bodies, the medial parts of the thalamus on each side, the inferior colliculi and, to some extent, the floor of the fourth ventricle. Throughout the midbrain and below the aqueduct of Sylvius in the pons were areas where the parenchyma was more or less loosely arranged and was undergoing subacute necrosis and where the capillary blood vessels appeared to be increased in size and in number.

The walls of the capillaries showed proliferation of their endothelial cells and of the cells in the surrounding elastic and fibrous layers. The changes in the walls of the capillaries appeared to be due to this proliferation (fig. 1 *A* and *B*). The perivascular spaces were enlarged in general in the areas affected.

In the localities of these parenchymal and vascular changes there were areas of old and fresh hemorrhage, which might be either extensive or rather small and which were perivascular. Old hemorrhage was usually indicated by the presence of pigment in the cells within the vicinity of the hemorrhage and in the perivascular spaces. The destruc-

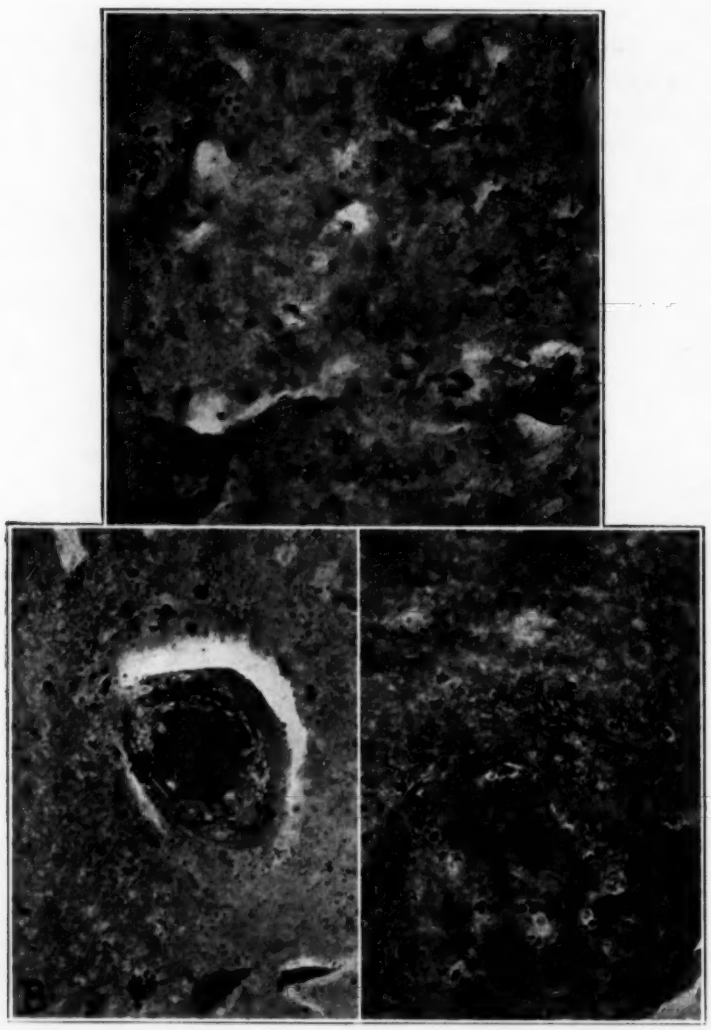

Fig. 1.—*A*, proliferation of the endothelial cells of the capillaries; *B*, loosely arranged capillary endothelium and pigmentary infiltration of nerve cells; *C*, extravasation of blood between endothelial cells of capillary. × 315.

tion of tissue might be so great as to obliterate the capillaries. In the areas of fresh hemorrhage the endothelial cells of the capillary vessels were loosely arranged (fig. 1 *B*). The blood cells of the exudates were scattered between the endothelial cells, through the perivascular spaces

and into the surrounding tissue (fig. 1 *C*). These hemorrhages were sometimes limited to the area about a capillary or sometimes so extensive as to cover an area approximately 1 to 10 mm. in diameter.

Focal areas of necrosis in the parenchyma varying in size from 1 mm. to several millimeters in diameter were also observed. Other areas were small and punctate, being only a fraction of a millimeter in diameter and scattered throughout a given area. There was no evidence of leukocytic infiltration except in case 3, as described hereafter.

Sections through the cortex showed no definite alterations in the cell arrangement or structure in any of the 5 cases studied and revealed changes in the leptomeninges in only 1 case. In the first case, the perivascular and pericellular spaces were enlarged. The leptomeninges showed chronic thickening and fibrosis. There were a marked degree of softening in the tissue beneath the pia mater, an increase in the endothelial cells of blood vessels in this region and extravasation of blood.

Special mention should be made of changes which were not characteristic of all the cases studied. In the second case small focal hemorrhages occurred in the medial nuclei of the thalamus in addition to the changes previously described. A section from the pons in the third case showed considerable leukocytic infiltration into the subarachnoid spaces and into the perivascular spaces. A very large area of hemorrhagic necrosis involved almost half of one side of the section. In the fifth case there were a number of small areas of hemorrhagic softening on one side in the pontile region.

Histopathologic Changes in Neurons and Axons.—Examination of microscopic sections of the midbrain and pons stained by the Cajal reduced silver method showed in all 5 cases focal neuronal degeneration within areas, or within the neighborhood of areas, of hemorrhage and necrosis.

Within the sections from these regions of the brain stem were to be seen nerve cells far removed from the areas of hemorrhage and necrosis in which there was infiltration of dark brown pigment throughout the cytoplasm of the cells. The pigment was of hematogenous character, originating from the disintegration of blood cells. It had probably been carried into the nerve cells in finely divided state during the process of absorption and was then condensed into granules within the cytoplasm (fig. 2 *A*). These cells had not undergone any apparent degeneration.

At the periphery of other areas of hemorrhage and necrosis nerve cells had undergone acute swelling or chromatolysis, some of which were in the more advanced stage of acute degeneration. Some of these cells also showed pigmentary infiltration (fig. 2 *B*). Where acute disintegration had taken place, the axons and dendrites had disintegrated

to a greater or less degree, and only fragments or granules of argentophilic material were visible (fig. 3 *C*).

Characteristic changes in the neurofibrillar apparatus, such as coarse and fine granulation, could also be discerned. These changes occurred in neurons at the margins of and within areas in which necrosis was

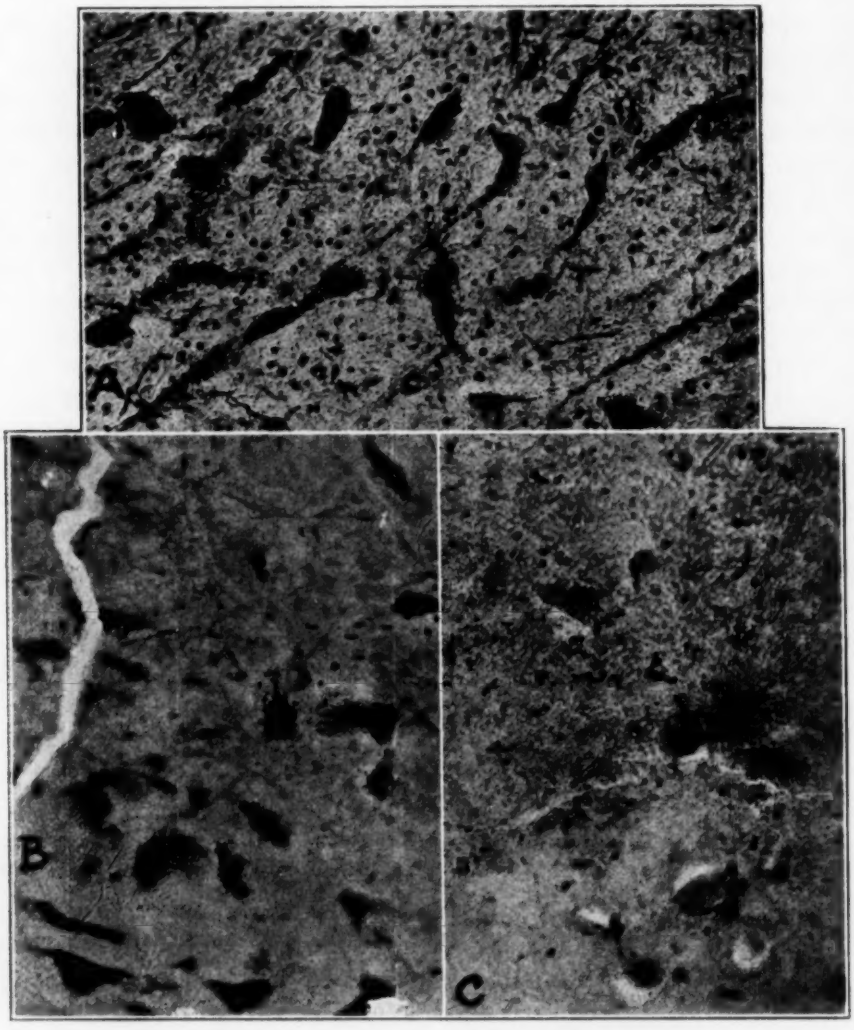

Fig. 2.—*A*, pigmentary infiltration; *B*, acute degeneration, and *C*, advanced degeneration, of nerve cells. × 358.

beginning or was under way. The cell in the early stage of change was not swollen, and its cytoplasm was filled with round, coarse, darkly stained granules. In later stages the cell might be slightly swollen, the cytoplasm was characterized by loss of detail and the nucleus might be slightly triangular. The cytoplasm of these cells contained fine

round granules in various groupings. In some cells the granules were collected in the center and the periphery was a clear zone (the hirudiform alteration of Cajal). In other cells there were fine granulations, with less seriously damaged fibrils along one border of the cell. Other cells

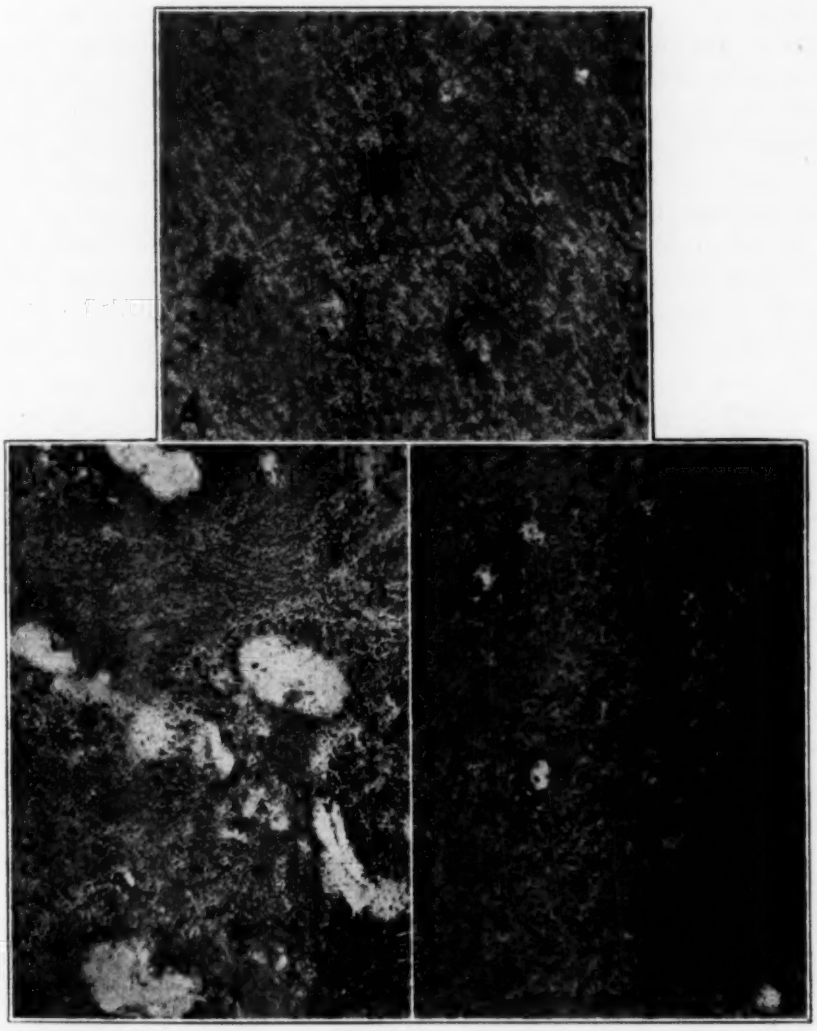

Fig. 3.—*A*, punctate necroses (× 300); *B*, fusion of necrotized spaces (× 300); *C*, complete destruction of neuronal elements (× 74).

showed coarse and fusiform degeneration of neurofibrils (fig. 2*C*). The extreme change in these cells consisted of an almost clear cytoplasm, containing a nucleus in the last stage of disintegration and very fine, darkly stained granules, which were irregularly and unevenly distributed. This series of changes in the nerve cells is known as hyalinization.

In addition to the hemorrhagic areas and areas of widespread necrosis, there were areas of punctate necrosis at various levels of the midbrain and pons. Many of these punctate areas were far removed from any hemorrhage and appeared in tissue in which the neighboring nerve cells had not undergone any degenerative changes. Each of these punctate spots of necrosis was surrounded with a ring of nerve fibers in which the silver stain had become much reduced. In some of these spots the center was deeply stained as well; in others the center contained shreds or strands of nerve fibers which were stained less deeply and formed a fenestra with a lattice-like arrangement of fibers (fig. 3 *A*). These punctate spots of necrosis were observed also in the hematoxylin-eosin preparations.

In some other areas of multiple punctate necrosis the necrotized spaces had retained their dark brown borders. In other areas the borders of these spaces had more or less broken down, so that they communicated with each other. Fine strands of nerve fibers, which had been spared from destruction, formed a delicate lattice work within these enclosures. There was also widespread acute disintegration of nerve cells in the surrounding areas (fig. 3 *B*).

In areas where complete destruction of all neuronal elements had occurred as a result of necrosis there was scattered a fine, darkly stained material, irregular in size and shape (fig. 3 *C*). Many of these areas were far removed from any site of hemorrhage and might or might not have punctate areas of necrosis within or near them.

Acute swelling and hyalinization of nerve cells are indicative of interference with the chemical processes in the tissue because of undernourishment and lack of oxygen supply. The mechanism underlying this process may be based either on an ischemia or a toxemia.

Histopathologic Changes in Neuroglia.—It was of particular interest to determine the nature of the reaction of the neuroglia in this study, as to my knowledge the reaction of the three neuroglial elements to the changes which take place in polioencephalitis hemorrhagica superior have not been reported fully. The reactions of the neuroglia to laceration and to mechanical injury have been studied extensively, both in animals and human beings.[5] There are other destructive processes, however, which take place in brain tissue resulting in regressive changes, which may be chronic or acute. The changes which had taken place in the tissues of these brains were evidently acute, resulting in focal necrosis, and were apparently the culmination of long-standing or chronic metabolic disturbances.

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5. del Rio-Hortega, P., in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 2. Rand, C. W., and Courville, C. G.: Histologic Studies of the Brain in Cases of Fatal Injury to the Head, Arch. Neurol. & Psychiat. **27**:1342 (June) 1932.

Astrocytes: The changes in the astrocytes were proliferative, degenerative and, to some degree, transformative. Proliferation of these neuroglial cells was prominent in certain areas, not necessarily around an area where tissue destruction was acute (fig. 4 *A*). It is

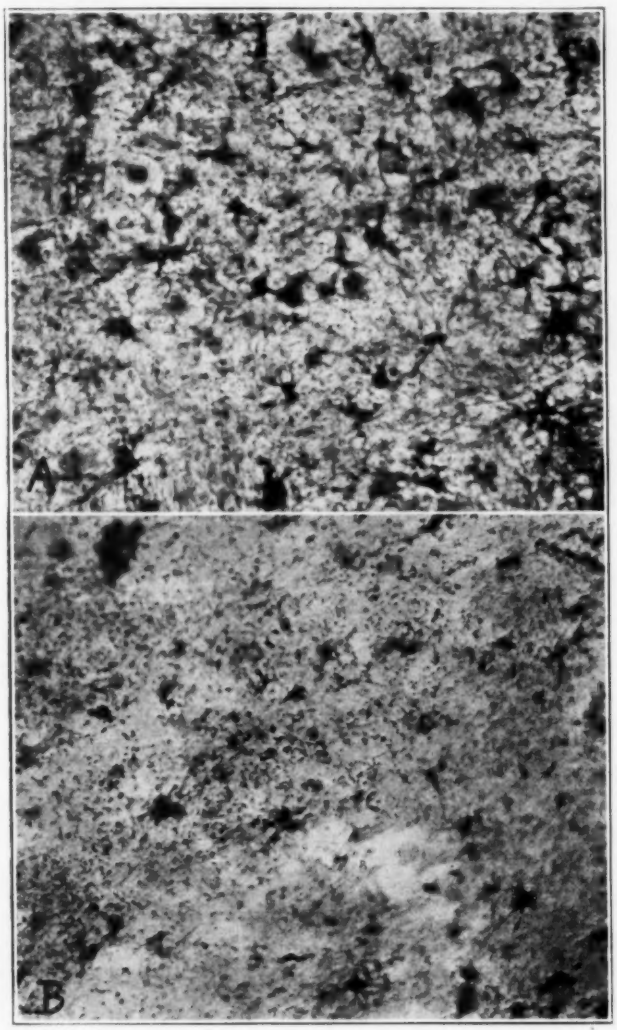

Fig. 4.—*A*, localized gliosis in area of necrosis; *B*, astrocytes undergoing degenerative changes. × 292.

indicative of stimulation by an irritative substance or by deprivation of blood supply.[6] The type of degeneration was that of acute destruction.

6. (*a*) Platt, B. S., and Lu, G. D.: Chemical and Clinical Findings in Beriberi with Special Reference to Vitamin B_1 Deficiency, Quart. J. Med. **5**:353, 1936. (*b*) Riggs, H. E., and Boles, R. S.: Wernicke's Disease, Quart. J. Stud. on Alcohol **5**:361, 1944.

The astrocytes in the midst of this acute destructive process were undergoing immediate and complete necrosis and clasmatodendrosis. At the periphery of such an area some of the astrocytes could be seen undergoing transformation (fig. 5 *A* and *B*). Many fibrous astrocytes were observed here, but occasionally astrocytes of the protoplasmic type could be seen forming neuroglial fibrillae. Transformation has been observed in degenerated areas following asphyxia.[7]

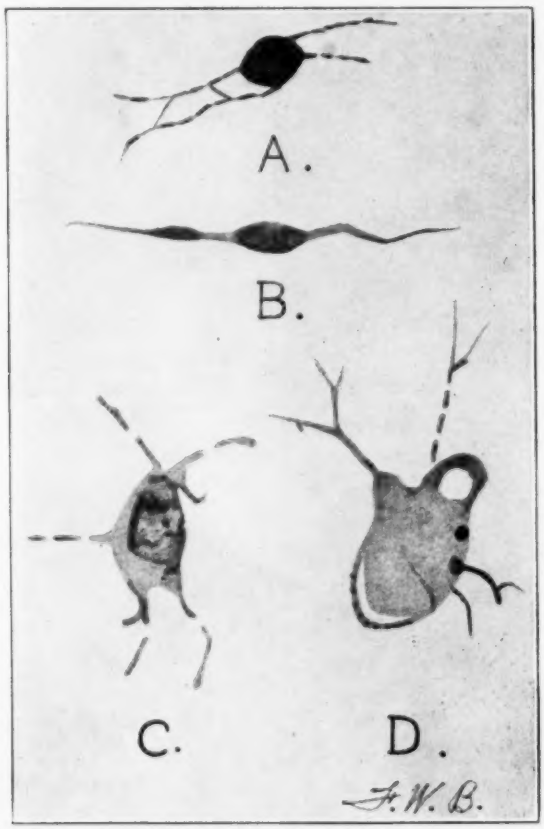

Fig. 5.—Pathologic changes observed in astrocytes. *A*, changes leading to formation of a pilonidal astrocyte; *B* and *C*, clasmatodendrosis of astrocyte; *D*, hyalinized, swollen astrocyte, or *gemästete Zelle*.

The astrocytes undergoing degenerative change were to be seen in the midst of the area of acute destruction which had undergone complete necrosis. The cell bodies not only had lost their processes but were fragmented and disintegrated. Astrocytes which had been killed but not destroyed had undergone a slower process of disintegration, namely, clasmatodendrosis (fig. 5 *C*). The cells had lost their processes

7. Courville, C. B.: Asphyxia as a Consequence of Nitrous Oxide Anesthesia, Medicine **15**:129, 1936.

by fragmentation, and the fragments had become granules. In some cells the cytoplasm contained granules; in others there were vacuoles, and in others there were both. No nuclei could be identified. The loss of the cell processes and the changes in the cytoplasm gave the cell an ameboid appearance, and this form has been termed the swollen

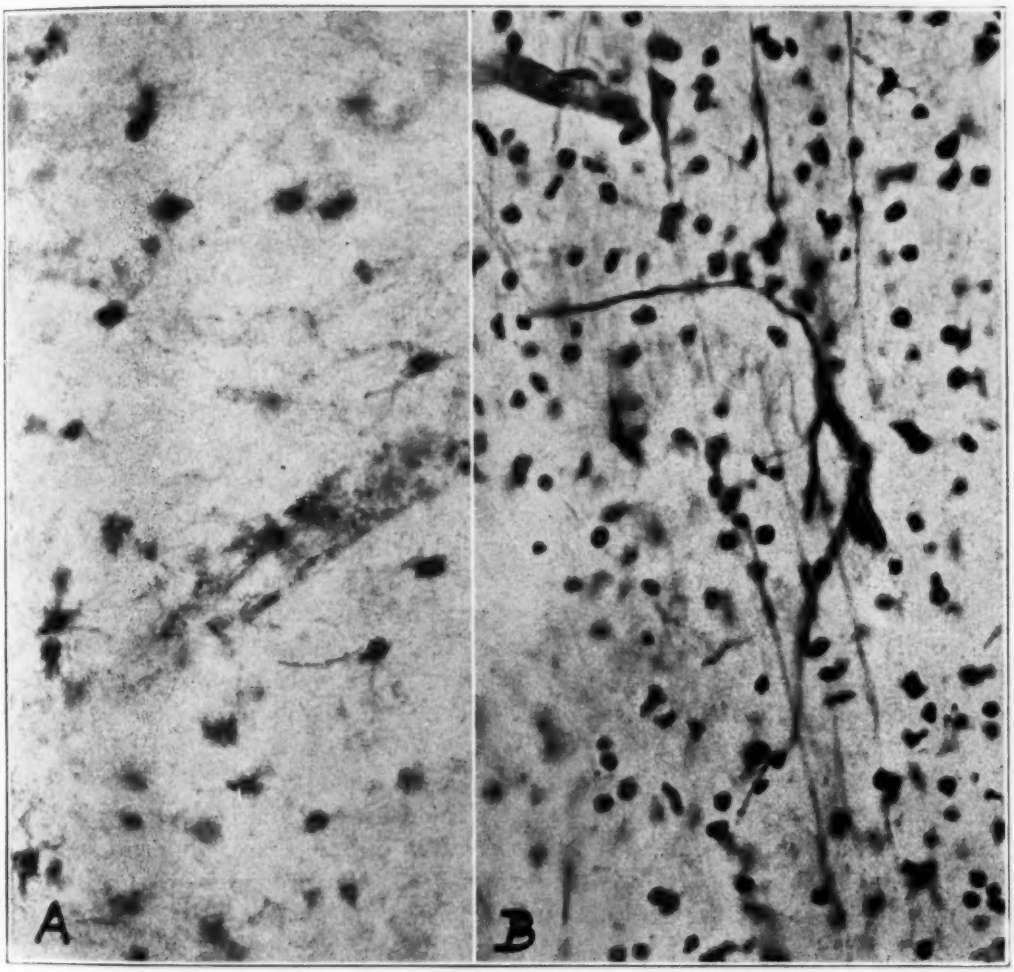

Fig. 6.—*A*, normal astrocytes and sucker feet; *B*, perivascular oligodendrogliosis. × 385.

astrocyte, or *gemästete Zelle*. It resembles the ameboid stage of the microglia cell (figs. 4 *B* and 5 *D*). The latter, however, has a definite nuclear structure within it.

The degenerative changes of the astrocytes were indicative of the rapidity and nature of the destructive processes. Cells which had undergone complete necrosis were indicative of areas of acute destruction,

whereas cells which were undergoing clasmatodendrosis were indicative of areas of slower destruction.

In other areas of these sections of the brain stem where the tissue was more normal, protoplasmic astrocytes could be seen. Some of these cells possessed long processes, the sucker feet, which extended to and were attached to blood vessels (fig. 6*A*).

Oligodendroglia: The changes in the oligodendroglia in response to the pathologic processes in this condition were chiefly those of acute swelling and of oligodendrogliosis (multiplication of cells) to a slight degree. These changes could be seen in areas undergoing partial or complete necrosis.

The phenomenon of acute swelling was characterized by marked enlargement of the cell, due to an accumulation of fluid within its cytoplasm in the form of vacuoles; the loss of cell processes, and nuclear pyknosis, the nucleus becoming central or eccentric in position. Acute swelling of the oligodendroglia cells was quite prevalent throughout the necrotic areas in the first and second cases, with coma of fourteen weeks and twelve days respectively before death, and, to a lesser extent, in the tissues in the other cases. Cell bodies undergoing hypertrophy, with increase of protoplasm and loss of cell processes preliminary to swelling, could be identified in both mildly necrotic and completely necrotic areas. Areas of moderate and complete necrosis contained cell bodies undergoing progressive hydropic swelling. The cell membrane appeared distended with clear fluid, through which extended strands of cytoplasm, while cytoplasmic granules were observed at the periphery. In some cells only granular fragments indicated where the strands were (fig. 7). The nuclear material in a large number of the cells was divided to form two, three and four masses. The processes extending from the cells were fragmented and in some instances had disappeared. Acute swelling has been observed before in pathologic conditions which have a toxic influence on the brain and appears to be an invariable accompaniment.[8]

In the first case there were tissues which contained areas undergoing partial necrosis in which perivascular oligodendrogliosis could be identified, appearing as concentrations of cells grouped about blood vessels (fig. 6*B*). This phenomenon did not occur in all areas of partial or complete necrosis. It is of interest to note that the first patient had been in a semicomatose state for three and a half months prior to her death. In the other cases studied the patients passed through periods of coma of much shorter duration. It is of significance that the phenomenon of perivascular oligodendrogliosis occurred only in this case of long-standing toxic state. It has been observed before in a

8. (*a*) von Meduna, L.: Beiträge zur Histopathologie der Mikroglia, Arch. f. Psychiat. **82**:123, 1927. (*b*) Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 2, p. 465.

variety of conditions, particularly in toxic encephalitis of childhood, and is thought to be the result of long-continued edema or toxic state.

Microglia: The microglial cells appear to be scattered at random in the nerve tissue, but there are other cells which are located near nerve cells (neuronal satellites), blood vessels (vascular satellites) and astrocytes (neuroglial satellites). The first two structures were identified in the tissues studied. The third was not identified. The microglial cells actively intervene in all inflammatory and necrotizing

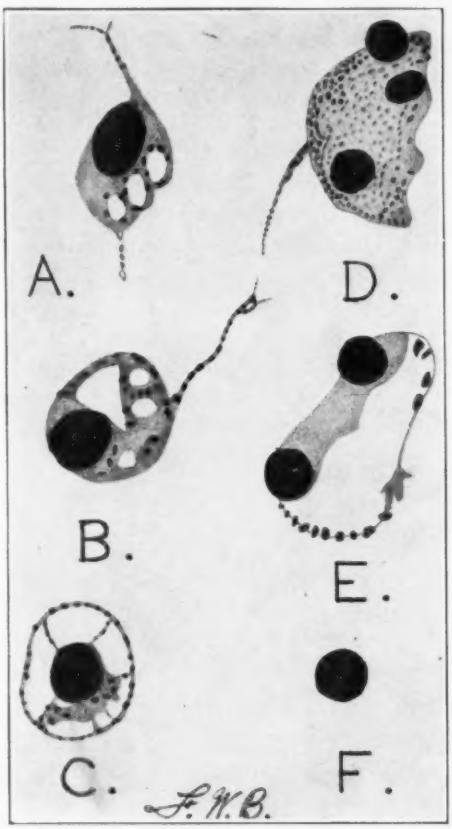

Fig. 7.—Acute swelling of oligodendroglia, showing the various stages from earliest swelling to destruction of the cell. *A*, early stage of hypertrophy; *B* and *C*, stages in swelling of the cell; *D*, cell division; *E*, destruction of cell; *F*, nucleus left after destruction of cell.

processes in nerve tissue. As a result of their motility and function as macrophages, they undergo three types of change: acute swelling, formation of rod cells and formation of compound granular corpuscles.

Examination of the tissues stained with the Penfield combined method showed normal microglial cells in the normal areas. In the areas of rapid degeneration, as in the areas of focal necrosis, normal microglia cells

were observed at the edge of, and occasionally within, the necrotic focus. Evidently, the pathologic change that occurred in such areas took place so rapidly that the microglia in these areas had not had enough time to undergo change. The microglia cells, including the neuronal and vascular satellite cells within the areas of focal necrosis, passive congestion and fresh hemorrhage, showed no pathologic changes or reactions.

In areas of ischemia and early to advanced generalized necrosis, acute swelling of microglia and formation of rod cells to some extent were observed.

Acute swelling is the first visible change in the microglia cell in any destructive lesion of nerve tissue and consists in an increase in volume, affecting first the cell processes and then the body. The processes of the microglial cells observed became transformed into thicker processes, which lost their spines and tended to become knotty and to form vacuoles. A later stage was observed in which the dendrites were still shorter and thicker and the cell body more swollen. Microglial cells undergoing acute swelling were numerous in areas of ischemia and early necrosis (fig. 8 *A*).

There could be seen also the occasional microglial cell which was becoming elongated to form a rod cell. The processes at the sides of the cell body were undergoing retraction and disintegration, while the processes from the opposite poles were preserved. These rod cells were seen within or at the periphery of areas of ischemia and early necrosis.

Acute swelling of microglial cells and formation of rod cells have been stated by some investigators to be produced by endogenous intoxication or by acute infection.[8b] However, previous destruction of the nerve structures is required for these reactions on the part of the microglia, and such a condition has been observed in very acute intoxications. The acute swelling of the microglia cells in these cases of polioencephalitis hemorrhagica superior is another instance of their response to an acute intoxication, accompanied with destruction of nerve tissue. The toxins produced are of endogenous origin. In exogenous intoxications no changes in the microglia have been observed.[9]

In areas of advanced necrosis and hemorrhagic areas of some duration the formation of compound granular corpuscles and their phagocytic action could be observed (fig. 8 *B*). The transformation of microglial cells into compound granular corpuscles consists in a series of changes. First, there is an increase in the cytoplasm of the cell, followed by enlargement with shortening and swelling of the expansions. The cell body becomes vacuolated; some of its expansions drop off, and

9. de Villaverde, J. M.: Lesions du cervelet dans l'intoxication par le plomb, Trav. du lab. de recherches biol. de l'Univ. de Madrid **25**:41, 1927. von Meduna.[8a]

it assumes an ameboid appearance, with short blunt processes. The cell finally assumes a globular shape, after it has ingested debris formed as a result of tissue destruction, to form the compound granular corpuscle. These various stages were present in the hemorrhagic areas with necrosis and in the areas of advanced necrosis in the tissues which were studied

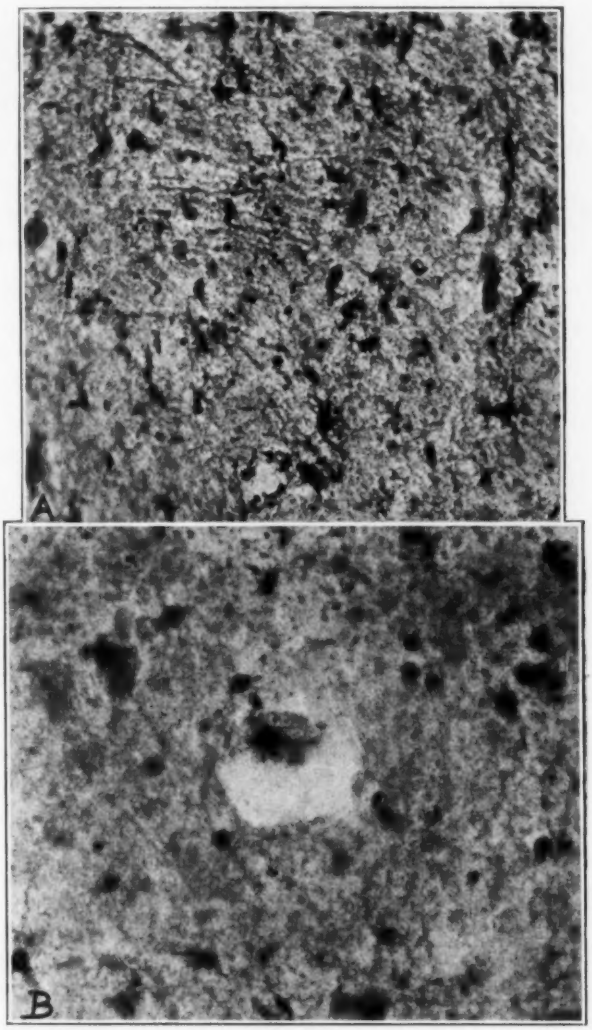

Fig. 8.—*A*, microglial cells undergoing acute swelling; *B*, compound granular corpuscles containing phagocytosed material. × 256.

(figs. 8 *B* and 9). In areas where there was hemorrhage but no necrosis no microglial changes were evident. It was observed, however, that the microglial cells within or close to the area of destruction were the first to undergo transformation and become phagocytic.

Careful study of all the areas of destroyed tissue showed no actual migration of compound granular corpuscles into them. In these areas there was an increase in the number of the phagocytic ecIls, but it was apparently due to the transformation of the microglial cells already there, for it was obvious that no normal microglial cells were present (fig. 8*B*). Instead of the normal microglial cells, the various stages

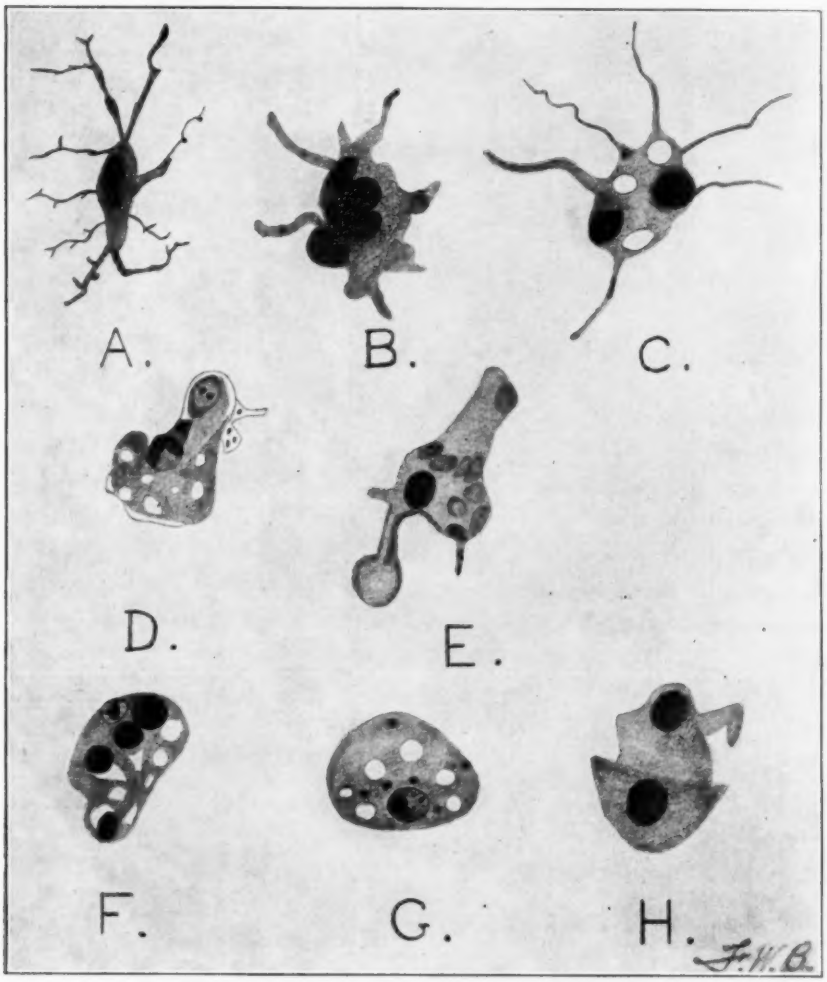

Fig. 9.—Changes in the microglia cell during its phagocytic activity. *A*, cell with rough long processes; *B*, cell with enlarged cell body and smooth, short processes; *C*, hypertrophic cell with pseudopodia; *D*, ameboid form; *E*, ameboid form containing granules of ingested material; *F*, globular form containing phagocytosed erythrocytes; *G*, compound granular corpuscle; *H*, corpuscle dividing.

of these cells could be seen, such as the acutely swollen cell with pseudopodia, the ameboid cell and the globose cell (the compound granular corpuscle) with ingested debris and blood cells. Mitotic

division of some of these cells could be observed occasionally, and increase in the number of these phagocytic cells in a given area was evidently also based on division of these cells.

In the destroyed or degenerated areas of the brain studied the compound granular corpuscles could be seen in the process of phagocytosing red blood cells and the degenerated products of necrosis. In old hemorrhagic areas a very small number of these ameboid cells were observed to have erythrocytes within them. Such cells were located within areas where there were small capillary hemorrhages with capillary budding. In the areas of massive hemorrhage no phagocytosis was observed. It appears that the hemorrhage was of such a sudden and extensive nature that the microglia had not had time to assume the phagocytic function.

The macrophagic function of the microglia evidently takes place slowly, by its metamorphosis, to form compound granular corpuscles. This neuroglial element undergoes modification during intense inflammatory conditions, during local disintegration of nerve tissue and apparently where there is hemorrhage of the exudative type of some duration.

PATHOLOGIC MECHANISM OF PRODUCTION OF LESIONS

The reactions of the various cellular elements are indicative of responses to the stimuli from toxic substances, from focal necrosis and from local hemorrhage which are produced by chemical changes in the tissues.

In view of the fact that thiamine deficiency contributes to polioencephalitis hemorrhagica superior, even when other vitamins are fed, the chemical factors which underlie this condition are to be considered. Funk [10] suggested that thiamine has some role in the metabolic transformation of carbohydrate in the animal body. Further studies indicated that a high carbohydrate diet is much more effective in producing the symptoms of thiamine deficiency than one high in fat. Westenbrink [11] suggested that during carbohydrate and fat metabolism thiamine is used at the same rate but when carbohydrate alone is metabolized a toxic metabolite arises which in the absence of the vitamin is not removed and which induces Wernicke's syndrome.

Lactic acid is a normal intermediate metabolite, which, in turn, produces pyruvic acid in the metabolic breakdown of glucose. Pyruvic acid is broken down by oxidative processes. Investigations have shown

10. Funk, C.: Studien über Beriberi: II. Die Rolle der Vitamine beim Kohlenhydratstoffwechsel, Ztschr. f. physiol. Chem. **89**:378, 1914.

11. Westenbrink, H. G. K.: Ueber den Einflusz der Menge und der Zusammenstellung der Nahrung auf die Folgen von Vitamin-B_1 Mangel, Arch. néerl. de physiol. **19**:94, 1934.

that associated with thiamine deficiency there is an accumulation of pyruvic acid in the blood which is proportional to the deficiency.[12] It can be reduced to normal by feeding thiamine (Platt [6a] and Thompson [13]). On the basis of these results, it is contended that thiamine brings about the oxidation of pyruvic acid and facilitates the absorption of oxygen by the tissues. The fasting level of pyruvate in the blood is invariably elevated in cases of thiamine deficiency, and after it is supplied the fasting level of blood pyruvate rapidly returns to normal. There is clinical improvement also. [14]

It is evident that in the state of chronic alcoholism, in which there are a deficiency of food intake and a disturbance of nutrition, thiamine deficiency occurs. This deficiency causes a faulty carbohydrate metabolism, with decrease in the amount of oxygen supplied to the tissues. The deficiency of oxygen and the accumulation of pyruvic acid produce anoxia and necrosis in the tissues. As a result of anoxia, the walls of capillaries become hypotonic. The endothelial cells proliferate, which is the result of an attempt at capillary budding. The attempt is soon aborted; the cells grow irregularly, instead of in the form of capillaries, and the walls become weak and varicose. The parenchyma of the brain tissue takes on a loose appearance, for the reason that the cells are unable to secure enough oxygen so that they can develop from carbohydrate sufficient energy to perform their various and specialized functions.

The more advanced states of focal necrosis, hemorrhage into the perivascular spaces and rupture of capillaries, are a result of further and prolonged interference with the normal function of the cells in the tissues and capillaries. The effect of the anoxia and the toxic metabolites, together with the inability of the cells to derive sufficient energy from carbohydrate metabolism, is to decompose and interfere with the production of the intercellular substance of tissues in general. The result is that the endothelial layer and the collagenous fibers which ensheath the capillaries become weakened and allow extravasations of blood and areas of degeneration and focal necrosis to develop in the parenchyma.

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12. Peters, R. A.: The Biochemical Lesion in Vitamin B_1 Deficiency, Lancet **1**:1161, 1936.

13. Thompson, R. H. S., and Johnson, R. E.: Blood Pyruvate in Vitamin B_1 Deficiency, Biochem. J. **29**:694, 1935.

14. Jolliffe, N.; Wortis, H., and Fein, H. D.: The Wernicke Syndrome, Arch. Neurol. & Psychiat. **46**:569 (Oct.) 1941. Wortis, H.; Bueding, E.; Stein, M. H., and Jolliffe, N.: Pyruvic Acid Studies in the Wernicke Syndrome, ibid. **47**:215 (Feb.) 1942.

SUMMARY AND CONCLUSIONS

1. The histopathologic processes underlying polioencephalitis hemorrhagica superior (Wernicke syndrome) are confined to the periventricular gray matter of the midbrain and pons, as well as the thalamus and the hypothalamus.

2. These processes consist of focal areas of small capillary hemorrhages and of necrosis. Vascular disturbances include dilatation of the capillaries, capillary budding and perivascular hemorrhages. There is parenchymatous degeneration, consisting of loosening of the ground substance.

3. Areas of widespread necrosis, of focal necrosis and of punctate necrosis occur. Within and near these areas there is neuronal degeneration, exhibiting acute swelling and hyalinization, changes indicative of interference with the chemical processes of the tissue due to lack of oxygen or inadequate elimination of toxic metabolites.

4. The astrocytes show proliferation, transformation and degeneration. Proliferative and transformative changes are indicative of widespread stimulation of the astrocytes by an irritative substance or by deprivation of oxygen supply. The degenerative changes of the astrocytes are indicative of the rapidity and nature of the destructive processes.

5. The changes in the oligodendroglia, which occur in areas undergoing partial or complete necrosis, are chiefly those of acute swelling and oligodendrogliosis. Acute swelling of oligodendroglial cells has been observed previously in pathologic conditions which exert a toxic influence on the brain and appears to be an invariable accompaniment of such states. The occasional occurrence of perivascular oligodendrogliosis in the tissues of the brain stem of patients who were in a semicomatose condition for long periods is indicative of a state of long-continued edema and toxemia.

6. In areas of ischemia and in areas of early to advanced necrosis, acute swelling of microglia and formation of rod cells to some extent are observed. Previous destruction of the nerve structures is required for this reaction on the part of the microglia, and such a condition is observed in polioencephalitis hemorrhagica superior, which arises from a condition of acute intoxication. The toxins produced are of endogenous origin, although the causative agent, alcohol, is an exogenous one.

In areas of advanced necrosis and in hemorrhagic areas of some duration the formation of compound granular corpuscles and their phagocytic action can be observed. In such areas there is an increase in the number of these phagocytic cells, but this is apparently due to the transformation of the microglial cells already there. There is no

evidence of migration of these phagocytic cells into the areas of destroyed tissue.

7. Underlying the histopathologic processes there is a deficiency of nutritional factors, the chief of which is thiamine. A number of investigators of this syndrome have demonstrated that there is interference with carbohydrate metabolism and with oxidation of pyruvic acid and that there is a decrease in the amount of oxygen supplied to the tissues. The effect of the anoxia and the toxic metabolites is to interfere with the chemistry of the cells and to cause their degeneration, which results in necrosis of various degrees in the tissues of the brain stem and in weakening of the walls of the capillaries, with extravasation of blood.

Presbyterian Hospital.

CAPILLARIES IN THE FINGER NAIL FOLD IN PATIENTS WITH NEUROSIS, EPILEPSY AND MIGRAINE

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MICROSCOPIC studies of the capillaries of the skin in living persons go back to 1922, when Otfried Müller, in Germany, published his book.[1] His studies did not concern the subject in which I have been interested. He investigated the morphologic changes and the blood flow in capillaries of the skin in physical disease, such as disturbances of the heart and kidneys. However, he and one of his co-workers, Parrisius,[2] have already described structural and functional abnormalities in so-called "vasoneurotic" patients.

The term "vasoneurotic" is somewhat vague; so no clearcut relation of the findings of these authors to the now better established types of the neuroses can be given. Some of their observations, especially on the structural abnormalities, agree with mine; others should be related, rather, to one group of neurotic patients only. However, a great many of their observations on the abnormalities of the blood flow are, according to my studies, not characteristic of patients with vasoneurotic disorders, since one can find them also in normal persons.

It is difficult to determine the subjects who can be used as normal controls for observations on neurotic persons because normal persons may have one or another trait found also in neurotic patients. I examined the capillaries of 125 so-called normal persons. The group consisted of students of Tufts College Medical School, of nurses of the Pratt Diagnostic Hospital, of some physicians and of patients who had been in the hospital for reasons other than neurotic or neurologic troubles. Of course, a number of those subjects, especially the students, were neurotic. I did not know this prior to my examinations. I exam-

This research was supported by a grant from the Harrington Fund.

From the Joseph H. Pratt Diagnostic Hospital and the Boston Dispensary.

1. Müller, O.: Die Kapillaren der menschlichen Körperoberfläche in gesunden und kranken Tagen, Stuttgart, Ferdinand Enke, 1922.

2. Parrisius, W.: Kapillarstudien bei Vasoneurosen, Deutsche Ztschr. f. Nervenh. **72**:310, 1921. Müller, O., and Parrisius, W.: Die Blutdruckkrankheit: Klinische, erbbiologische, anthropometrische, biochemische, histologische, kapillarmikroskopische und andere Untersuchungen am Blutumlauf bei Hypertonikern, Stuttgart, Ferdinand Enke, 1932.

ined the capillaries before I had interviewed the subject for the presence of neurotic traits. Ninety-three per cent of these normal persons had normal capillaries; 7 per cent showed the anomalies seen in neurotic patients. Therefore one can state with certainty that there exists a normal capillary picture in adult normal persons. I emphasize the word "adult," because children show a different capillary picture. There is a fairly regular change with age, although the development of the capillary picture from that of the newborn to the final pattern of the grown-up differs with different persons. It depends not only on the anlage of the ectoderm but probably also on environmental factors.

Studies on the development of the capillaries in children were the starting point of my investigations, which go back a number of years. It was Jaensch [3] who first inaugurated these studies and, together with two other authors, Hoepfner and Wittneben, published a book on his observations in 1929. In America, Powdermaker [4] published the results of corresponding examinations in the same year, and Leader [5] reported her observations in 1932. All these studies show that there is a rather strict relation between the development of the capillary picture and the mental development. For instance, examinations by German investigators showed that the capillaries of 67 per cent of children in a normal school displayed a normal pattern, whereas only 29 per cent of children of an ungraded school showed normal capillaries. Powdermaker obtained corresponding figures, and, what is more interesting, she did not find abnormal capillaries in those retarded children whose defectiveness was due to such factors as trauma, encephalitis and meningitis. She concluded that an examination of the capillaries may help to establish a diagnosis when the early history is inadequate to distinguish between a constitutional etiologic and an environmental factor. Similar were the findings of Leader, who observed normal capillaries in children with delayed physical development but with normal or superior intelligence. Another American author, Crawford,[6] went so far as to state that the capillaries are as characteristic in a given person as his face and that they remain essentially the same from day to day and from minute to minute.

This morphologic stability is true only in adults after the development of the capillaries has come to an end. As I mentioned before,

3. Jaensch, W.: Die Hautkapillaroskopie, Halle, Carl Marhold, 1929.

4. Powdermaker, F.: Capillary Forms in Relation to Certain Problems in Development, Arch. Neurol. & Psychiat. **22**:1207 (Dec.) 1929.

5. Leader, S. D.: Capillary Microscopy in Children, Am. J. Dis. Child. **44**:403 (Aug.) 1932.

6. Crawford, J. H.: Human Capillaries: Observations in the Capillary Circulation in Normal Subjects, J. Clin. Investigation **2**:351, 1926.

this end is different in different children. Powdermaker stated that the end stage may be reached as early as the age of 6 months or as late as 6 years. The German authors made the interesting observation that the development of the capillaries is delayed in children who grow up in a population in which goiter is endemic. Leader, in America, found that abnormal capillaries in myxedematous children developed rapidly in normal forms with thyroid medication.

The relation between retarded development of the capillaries and mental abnormalities in children is the only clue to the relation of the capillary pattern to the structure of the brain. The fact that the skin and the nervous system come from the same germinal layer does not mean much in this regard, especially as the capillaries originate in the mesoderm. Nevertheless, Jaensch expressed the belief that the evolution of the capillaries coincides with the myelination of the nerves and the differentiation of the cerebral cortex.

METHOD

I used an ordinary microscope with an eyepiece with a magnification of 7.5 and an objective lens with a magnification of 10. The best region for the observation of the capillaries is the finger nail fold. One can use other parts of the body, but the results are not so good, especially if one wants to make photographs. As the finger must be kept as steady as possible, I made a holder on the platform of the microscope with two walls, between which the finger could be kept in the proper place. By means of the two screws of the microscope table, the finger could be moved easily in all directions, which is necessary if one is to observe the capillaries in different parts of the finger. The skin just under the lens is covered with cedar oil in order to make it more transparent. One has to use a strong lateral light focused exactly on the spot of observation. I used a very strong electric bulb equipped with a special device at the side of the lens, so that it could be adjusted at different angles. This light, however, is not strong enough for making photographs. For photography I used an arc lamp with a green filter. This is necessary; otherwise one gets very poor pictures, such as are seen in most publications. One has to make very short exposures, as despite all fixation the patient is unable to keep the finger steady. The development of this technic is difficult and discouraging, but I found it necessary to spend much time on it, because drawings, such as have been used by most authors, are not convincing. Although I have succeeded in getting some good photographs, I must say that the microscopic observation is much more important. As the surface of the finger nail fold is curved, and not a plane, and as the capillaries are not all situated in the same layer, one has to focus up and down with the fine adjustment in order to see the whole structure of a capillary.

The visibility of the capillaries is dependent on the transparency of the skin. This differs with different persons, and even at different times. For instance, perspiration interferes with the visibility. Ordinary injuries of the fingers, with which I include manicuring, do not interfere with the visibility and the form of the capillaries. Environmental influences do not play any role. There are, however, a certain number of persons, approximately 10 per cent, with a skin too thick to permit good examination of the capillaries.

NORMAL ANATOMIC PICTURE

The capillaries of the nail fold show a deep arterial network; a second, subpapillary network near the junction of the middle and the outer third of the cutis, and a third, even more superficial, arterial network beneath the papillae. From this network arise the capillaries in the papillae. Between these arterial layers are at least four venous plexuses. Only one capillary loop is present in each papilla.

The normal development of the capillaries may be summarized as follows (fig. 1): At birth there are no capillary loops in the papillary layer. The upper part of the corium represents a flat line. There is a primitive network of vessels supplied by the arterioles and venules of

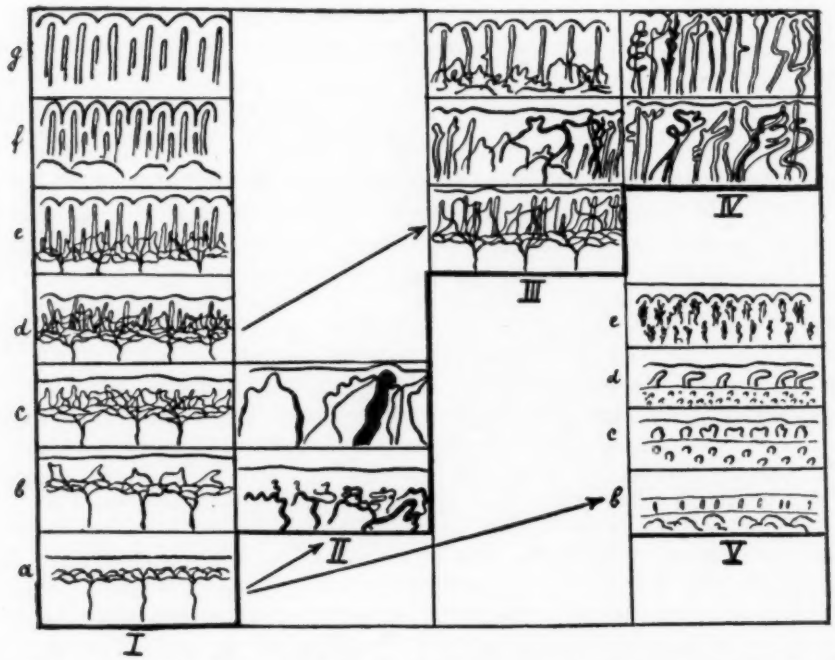

Fig. 1.—Development of capillaries in the newborn. The column at the left shows normal development (to be read from the bottom to the top). The other columns show arrested development in mentally retarded children. The arrows indicate the stage at which the development was arrested and went the wrong way.

the deeper layers. At the age of about 4 weeks saddle-shaped forms sprout from the primitive plexus. They grow gradually in the direction of the corium; but not before the fifth month does one find the hairpin-like capillary loops, each of which lies in a papilla. At the same time, the horizontal network of fine blood vessels decreases in size, and the corium becomes wavy. At the time when definite loops have developed, the corium assumes the scalloped appearance. At from the fifth or sixth month to one year of age the capillaries and the papillae develop into

the mature picture, as seen in *g* of figure 1. This figure, a drawing by Jaensch,[3] shows in the left column, which is to be read from the bottom to the top, the normal development of the capillaries in children. In the other columns, Jaensch has recorded the capillary patterns due to abnormal development in mentally retarded children. The arrows indicate at what stage the development has stopped. Column *V* shows a special hypoplastic, primitive stage, seen oftentimes in cretins. It is important to stress that at the end of normal development no horizontal network or subpapillary plexus can longer be seen.

The pattern of the normal capillaries in adults is as follows: The corium is well scalloped, and the papillae are rather regular. The capillaries of the first row are hairpin-like. The arterial limb is narrower than the venous limb. Figure 2 shows examples of normal capillaries. According to Müller, the width of the lumen is 0.009 to 0.012 mm.

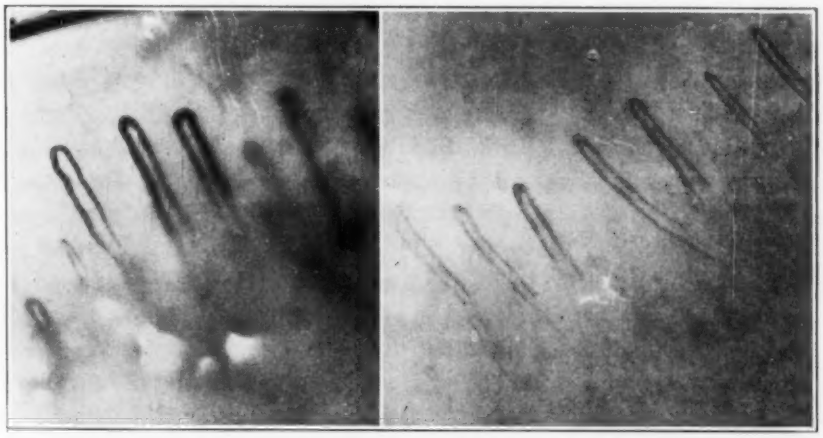

Fig. 2.—Normal capillaries in the adult. The photographs show the capillaries of the end row. They are hairpin-like, straight and evenly distributed.

My own figures are a bit higher—0.014 to 0.021 mm. These values correspond better than Müller's to the figures of Krogh,[7] who mentioned 0.02 mm. as the width. According to Deutsch,[8] who made capillary studies in cases of Raynaud's disease, the height of the capillaries is 0.2 to 0.4 mm. My own figures are smaller—0.04 to 0.1 mm. I do not believe that these differences are important, as the size of the capillaries differs in different persons. I got the impression that there is some relation to the anthropologic bodily structure (leptosomatic, pyknic, athletic).

7. Krogh, A.: Anatomy and Physiology of the Capillaries, New Haven, Conn., Yale University Press, 1924.

8. Deutsch, F.: Capillary Studies in Raynaud's Disease, J. Lab. & Clin. Med. **26**:1729, 1941.

It is important to stress that in normal adults no subpapillary plexus is visible. I emphasize this fact because the persistence, or, let me say more cautiously, the visibility, of a horizontal network of vessels in the proximal parts of the nail fold means, in my opinion, a pathologic pattern. Normally one does not see any connection between the capillaries in the first row and the deeper vessels.

The capillaries of the first row are not the only ones which are visible, although they are better visible, and their shape is more significant, than the capillaries of the proximal parts. Those capillaries are usually shorter, and they do not appear at the same angle as the capillaries of the first row. This may also be one reason for the shorter appearance, for one often looks vertically at the connecting part between the arterial and the venous limb.

The distribution of the capillaries is very even in normal subjects, especially in the first row. Irregularities in this regard are as significant as variations from the hairpin-like shape. Usually the capillary pattern is the same in all fingers and in both hands. I always studied the fourth and fifth fingers of each hand. The fourth finger is the best test object. On the little finger, even in normal persons, one is more likely to find variations in the distribution and form of the capillaries. Generally, in the little finger the abnormalities seen in the other fingers are magnified and multiplied. For instance, if there are a few abnormal structures in the fourth finger, one will find them more pronounced in the little finger. One never should examine one finger and one hand only.

Slight variations from the ideal pattern of the capillaries are not to be considered pathologic. If the variation concerned only a different shape of the capillaries in the end row, not the visibility of a horizontal network of vessels, I usually counted the number of abnormal capillaries in one visual field. This gave me the degree of abnormality, e. g., 5 or 10 per cent or more. The normal variations from the hairpin-like shape consist in some tortuosities or slight twisting or in figure 8 forms. If the abnormal forms exceed 20 per cent in a field, I do not consider the pattern normal. It belongs, then, in the category of the 7 per cent incidence of abnormal capillaries in normal persons, which I mentioned earlier.

OBSERVATIONS

Neurosis.—I examined 578 abnormal subjects. This number consisted of 375 patients with neurosis, 117 with epilepsy, 37 with migraine, 21 with nonmigraine headache and 28 with other neurologic diseases.

I divided the 375 neurotic patients into 304 constitutionally neurotic persons and 71 with neurotic reactions. I called those patients constitutionally neurotic in whose family several other neurotic persons could be found and who obviously had inherited their neurotic anlage. Another

evidence of their abnormal constitution could be seen in the fact that neurotic traits appeared very early in life and could not be explained by environmental factors, such as unhappy home conditions or troubles in school or in their relation to friends. Neurotic traits persisted throughout their life independent of environmental circumstances, or even despite favorable conditions. The patients with neurotic reactions, on the contrary, were not nervous *ab origine*. In their families usually no other neurotic persons could be found. They did not show neurotic traits during childhood, even when the family life or their experiences during "teen age" contained noxious agents. It was not difficult to relate their neuroses to definite environmental circumstances, such as marital or family trouble, severe grief, difficulties in business or serious sickness. Oftentimes those reactive neurotic traits disappeared in the course of time and the patient remained normal until a new troublesome experience caused a second neurotic reaction. It goes without saying that there is no strict borderline between these two groups of neurotic patients; one may be in doubt occasionally whether a patient should be put in the one or in the other group. It was interesting that of the 304 constitutionally neurotic persons, 268, or 88.1 per cent, showed abnormal capillaries, whereas only 36, or 11.8 per cent, showed normal capillaries. Of the 71 patients with neurotic reactions, however, only 3, or 4.2 per cent, showed abnormal capillaries, whereas 68, or 95.7 per cent, had normal capillaries.

The shape of the abnormal capillaries in neurotic patients can be seen in figure 3. The papillae are not regularly built; they do not stay in one row; sometimes they are very shallow, and in cases of severe neuroses there are no papillae at all. Also, the distribution of the capillaries is irregular. They do not stay in clearcut rows, and they are not all oriented in the vertical direction. The most characteristic anomaly, however, is the tortuosity. They are twisted and sometimes show grotesque forms. The twisting is not restricted to one of the limbs. The caliber of the capillaries is often large. The most pronounced twistings appear in the capillaries of the end row, or at least they are best visible there. A certain percentage of neurotic patients showed a pattern which is also seen in mentally retarded children, and, as will be seen later, in epileptic patients. This pattern consisted of horizontal vessels in the proximal parts of the nail fold, sometimes even of a horizontal network of vessels. Oftentimes the capillaries could be followed into this network. This pattern can best be interpreted as a primitive stage, known from the development of the capillaries in early childhood. Of 586 persons (normal subjects and patients with neurosis, nonmigraine headache and other neurologic diseases) I found this pattern in 73, that is, in 12.4 per cent. Interestingly, this immature picture was found especially in patients with

hysteria. This corresponds with my conception of hysteria as a neurosis of primitive structure. The most pronounced tortuosities could be found with anxiety neurosis.

The difference between the "constitutionally neurotic" patients and the patients with neurotic reactions is a strong one. That 88 per cent of the former and only 4 per cent of the latter had abnormal capillary pictures in the nail fold is certainly significant. It would seem to indicate that there is a developmental defect in the patients with con-

Fig. 3.—Abnormal tortuosities of the capillaries in constitutionally neurotic patients. The pictures show different forms and degrees of abnormally shaped capillaries of the end row.

stitutional neurosis which is absent in the patients classified as having only "neurotic reactions." The fact that the abnormal capillary picture is made up of peculiarly shaped capillary loops, or occasionally even of horizontal vessels, such as are seen in the early stages of normal development, indicates that the abnormality is congenital rather than acquired. The findings are not surprising. They merely support the conception of those authors who believe in the constitutional basis of

some neuroses and who do not believe that environmental factors always give the clue to an understanding of the neuroses. Examination of the capillary pattern might be a useful test in cases in which it is important to distinguish between anlage and morbid reaction, e. g., in the examination of would-be soldiers or employees for special work which requires

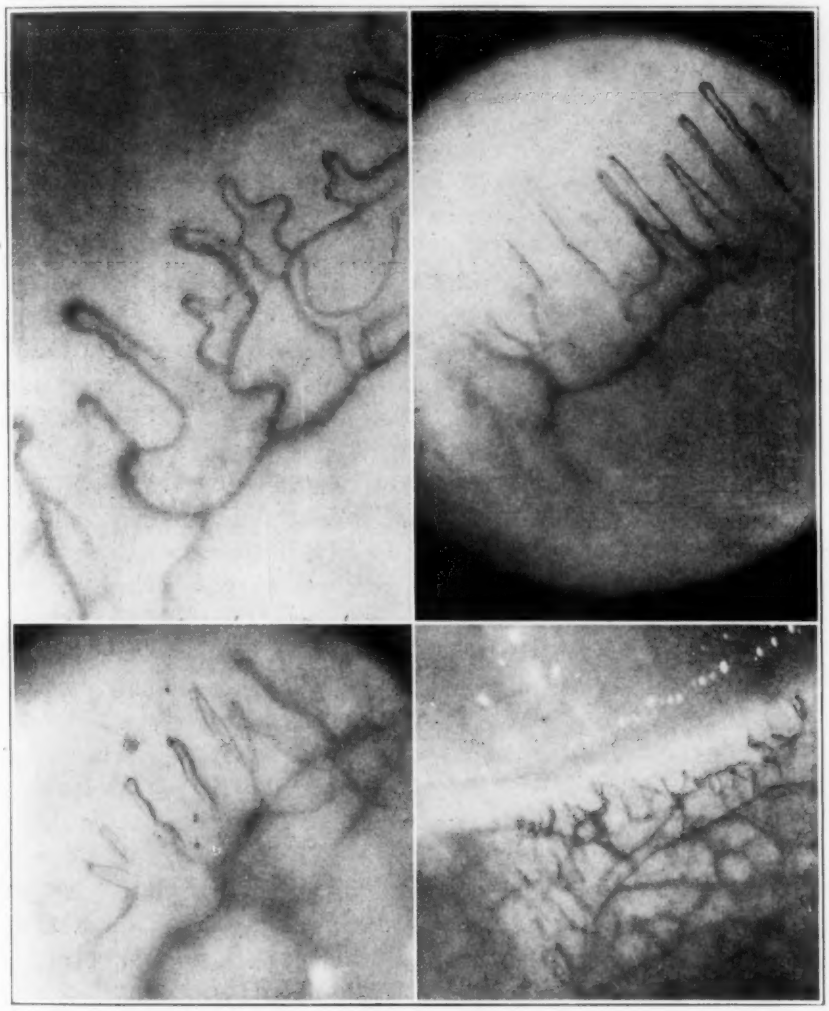

Fig. 4.—Immature capillary pattern in patients with idiopathic epilepsy. Horizontal vessels are visible in the more proximal rows, in *D* there is even a network of these vessels. One can follow the capillaries of the end row into these horizontal vessels.

a stable personality or in the examination of school children. The study of such objective somatic signs gives psychologic tests a broader basis.

Epilepsy.—I examined 117 patients with epilepsy; 73 of them may be said to have idiopathic epilepsy and 44 symptomatic epilepsy. I do

not have to stress that this differentiation is often difficult, or even impossible. In most cases I also made use of the electroencephalogram. The capillary picture was characterized by horizontal vessels, or even a horizontal network, in the proximal part of the nail fold (fig. 4). The capillaries of the end row did not show many anomalies. One could follow the capillaries of the end row into those horizontal vessels. It was an "immature picture," such as is seen in mentally retarded children. Further evidence was the presence of abnormally shaped capillaries, such as are seen during the early stages of normal development of the capillaries. Thus, it would seem that this pattern represents a retarded development of the capillaries or a development which came to a standstill before it was finished.

I found this capillary picture in 50 of the 73 patients with idiopathic epilepsy, that is, in 68.4 per cent. The figures for the patients with symptomatic epilepsy were quite different: Of 44, only 10 showed this picture—22.7 per cent. This is a significant difference in spite of the inevitable errors in diagnosis as to "idiopathic" and "symptomatic." One must consider the theory that even in symptomatic epilepsy there might be a specific cerebral predisposition which requires an additional exogenous factor in order to manifest itself in epileptic seizures. I do not like to say that the presence of those horizontal vessels is a positive diagnostic aid in questionable cases of epilepsy, for one can find them occasionally also in nonepileptic cases. Nevertheless, one can say that the absence of those vessels speaks strongly against idiopathic epilepsy (fig. 5).

Of the few capillary studies which I found in the literature, only two authors mention observations on epileptic patients. Olkon [9] described epileptic monozygotic twins and spoke of "thickened walls of the subpapillary plexus." This at least can be interpreted as evidence of the visibility of such a plexus. Leader [5] examined 12 patients with epilepsy; in 2 she saw evidence of retarded development, namely, bizarre shapes, subpapillary plexus and irregular corium. In 2 others she noted the pattern of "vasomotor instability." She did not distinguish between idiopathic and symptomatic epilepsy, but even so her observations represent some support of my own.

Migraine.—I studied the capillary pattern of patients with migraine because of the well known relationship between epilepsy and migraine. I examined 37 such patients. In my opinion, the diagnosis of migraine is made much too often. My patients had true migraine, I believe, although, of course, there might be some cases which another examiner would put in a different category of headache. The same holds true

9. Olkon, D. M.: Epilepsy of the Angiospastic Variety in Monozygotic Twins, Arch. Neurol. & Psychiat. **25**:1111 (May) 1931.

Fig. 5.—Normal capillary pattern in a patient with symptomatic epilepsy, showing hairpin-like, straight, evenly distributed capillaries in three rows.

Fig. 6.—Immature capillary pattern in a patient with migraine, showing horizontal vessels in the proximal row, in connection with the capillaries in the end row.

for the 21 patients with nonmigraine headaches; in these 21 patients the main symptom was headache. Of the 37 patients with migraine, I found a picture (fig. 6) like that accompanying idiopathic epilepsy in 20, that is, in 54 per cent, whereas none of the patients with nonmigraine headache showed this capillary picture. This is in accord with the concept that migraine and epilepsy grow on the same tree. Of course, 54 per cent is a figure too low to enable one to state that migraine has a typical capillary picture; however, when it is compared with the 14 per cent of similar changes in all the other patients examined, it indicates an abnormal anlage of the capillaries of the peripheral vessels. This may be true of the brain, provided the capillary pattern of the finger nail fold permits one to draw any conclusions concerning the cerebral capillaries.

Recently, studies of the capillaries of the fingers in patients with migraine have been published by Redisch and Pelzer.[10] These investigations were concerned, however, with the impaired visibility of the capillaries during an attack of migraine and the effect of ergotamine tartrate, rather than the form of the capillaries.

SUMMARY

1. There exists a characteristic "normal" pattern of the capillaries of the finger nail fold in adult "normal" persons.

2. The immature capillary picture of the newborn develops to the mature end stage, which can be reached as early as 6 months or as late as 6 years of age.

3. This normal development is arrested at various stages in mentally retarded children.

4. Constitutionally neurotic patients showed an abnormal capillary picture, consisting mainly in tortuosities of the normally hairpin-like capillaries in 88 per cent. Patients with neurotic reactions, on the other hand, showed this picture in only 4 per cent. Therefore, examination of the capillaries furnishes a means of detecting persons of neurotic predisposition.

5. Patients with idiopathic epilepsy display an immature capillary picture, similar to that seen during the normal development of the capillaries in early childhood, before the end stage is reached. Patients with symptomatic epilepsy show this pattern to a much less degree.

6. Migrainous patients show a capillary picture similar to that of epileptic patients.

Joseph H. Pratt Diagnostic Hospital.

10. Redisch, W., and Pelzer, R. H.: Capillary Studies in Migraine, Am. Heart J. **26**:598, 1943.

CAPILLARIES OF THE NAIL FOLD IN PATIENTS WITH NEUROCIRCULATORY ASTHENIA (EFFORT SYNDROME, ANXIETY NEUROSIS)

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AS PART of an extensive study [1] of neurocirculatory asthenia, in which many methods of examination were used, the capillaries of the nail fold were examined in 48 patients with neurocirculatory asthenia [2] and in 44 normal controls. It has long been known that persons with peripheral vascular disease have abnormal capillaries that can be seen in the nail fold and that in certain cases of mental defect,[3] "vasomotor neurosis,"[4] epilepsy and migraine variations from the normal capillary picture occur.[5] Recently Hauptmann[6] has thoroughly reviewed the literature and has shown that in many patients with psychoneurosis, especially anxiety states and hysteria, the capillaries are abnormal. He has helped us in our study by showing us his material, by advising as to our technic and by making photographs for us.

METHOD

With the 92 persons included in this study the usual procedure was to examine the nail fold of the fourth finger of each hand. If the cuticle was thick and the visibility bad, another finger was sometimes used. The area to be examined was lightly sponged off with an alcohol-ether mixture to remove oily deposits. Then, after the finger was placed in the holder beneath the lens, a drop of cedar oil was

From the Massachusetts Branch of the Hall-Mercer Hospital.

The work described in this paper was done under a contract, recommended by the Committee of Medical Research, between the Office of Scientific Research and Development and the Massachusetts General Hospital.

1. White, P. D.; Cobb, S.; Chapman, W. P.; Cohen, M. E., and Badal, D. W.: Tr. A. Am. Physicians **58**:129, 1944.

2. For a definition of neurocirculatory asthenia, see article cited in footnote 1.

3. Potosky, C.: Am. J. Ment. Deficiency **47**:167, 1942.

4. Parriseus, W.: Deutsche Ztschr. f. Nervenh. **72**:310, 1921. Parriseus' figure 5 is comparable to the pattern for our normal controls and his figure 15 to the pictures for 4 patients with neurocirculatory asthenia.

5. Paskind, H. A., and Brown, M.: Constitutional Differences Between Deteriorated and Nondeteriorated Patients with Epilepsy, Arch. Neurol. & Psychiat. **49**:49 (Jan.) 1943.

6. Hauptmann, A.: Capillaries in the Finger Nail Fold in Patients with Neurosis, Epilepsy and Migraine, Arch. Neurol. & Psychiat., this issue, p. 631.

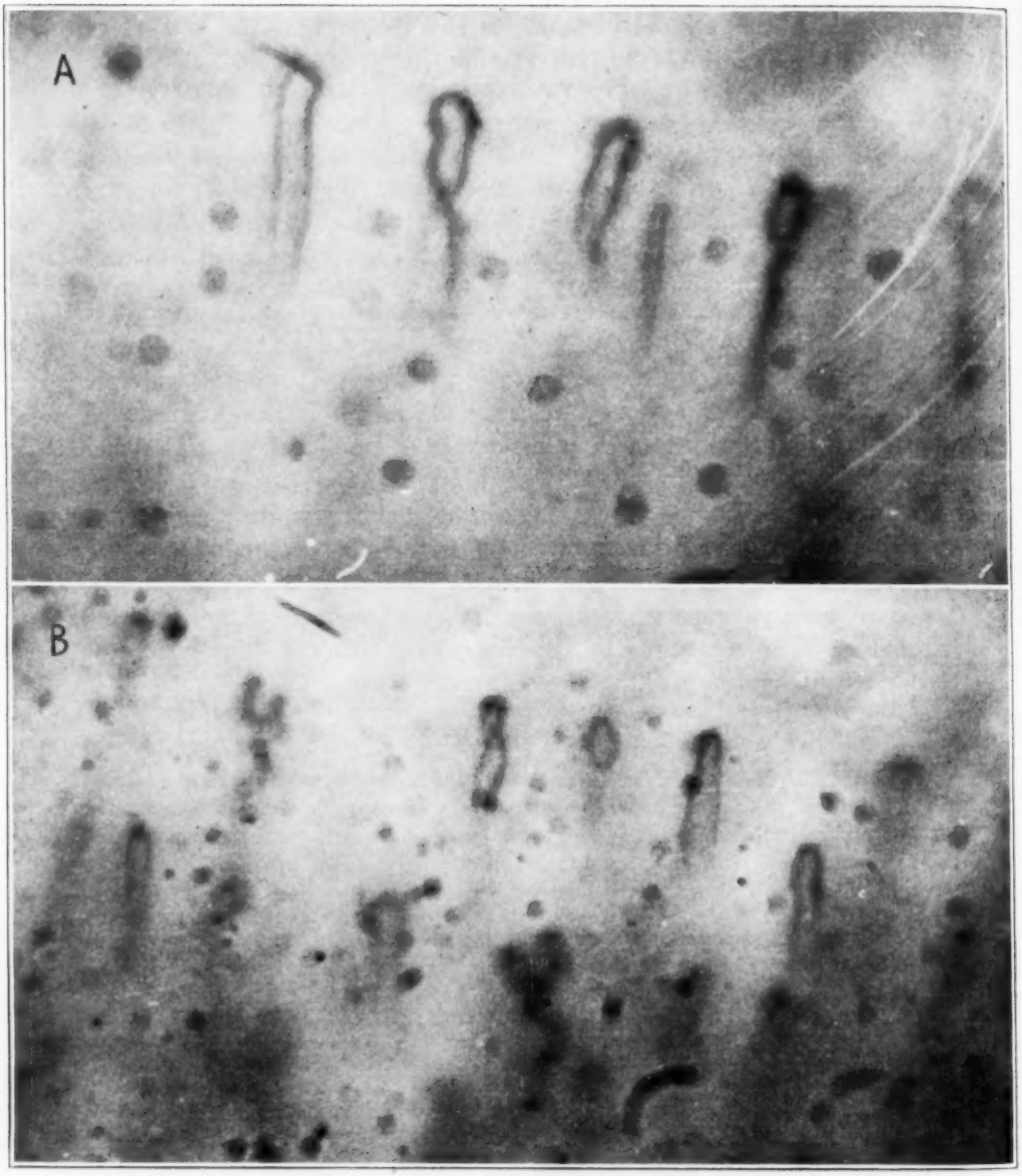
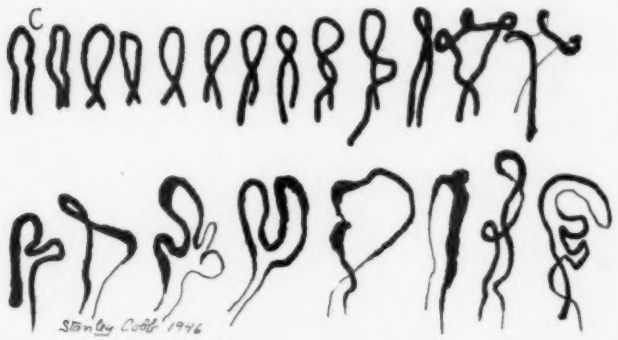


Fig. 1.—*A*, photomicrograph of capillaries at the edge of the nail fold of a patient with neurocirculatory asthenia. Of the 9 capillaries in focus in this plane, it can be seen that 3 are simple loops and 6 are more complex in form. Magnification, about 200.

B, 5 capillaries along the edge of the nail fold; 3 are simple, hairpin loops, and 2 are the more complex form described in the text.



C, drawings of capillary loops selected from several patients to show variations in form. The first 4 in the upper row would be called hairpin forms in spite of a slight crossing at the bottom. The fifth loop is equivocal, and the next 8 are definitely looped forms. The lower row shows some of the many complex forms.

spread over the junction of the cuticle and the nail at a point where it seemed smooth and flat. The observations were made with a Zeiss capillary microscope with a no. 8 objective and a no. 6 ocular, giving a magnification of about 48 diameters. The field was illuminated with a strong, laterally directed electric lamp focused through two lenses, a water filter for coolness and a light green filter.

When the capillaries in the edge of the cuticle were brought into focus, an area was found where the outermost series of loops could be seen clearly. With averaged-sized capillaries normally spaced, one microscopic field would take in 12 to 14 loops, arranged usually in a somewhat regular row across the field. One or two such fields can be found in most nail folds, and the first good one found was used. A series of 10 capillary loops was then drawn on paper by the observer. The same procedure was followed with the other hand. The drawings were labeled and filed with the patient's record.

In making counts from these drawings, the capillaries were at first divided into morphologic types representing (*a*) simple, hairpin-shaped forms; (*b*) looped forms in which the arterial arm crossed the venous arm one or more times, making a closed loop at the end, and (*c*) irregular, branching forms, fanlike ameboid,

Percentage Incidence of Simple Hairpin and Complex Capillary Loops in the Finger Nail Fold in 48 Patients with Neurocirculatory Disturbances and in 44 Controls

	Simple	Complex
Patient with neurocirculatory asthenia		
Chronic (32)	44	56
Acute (16)	47	53
Controls		
Normal (23)	79	21
Osteomyelitis (21)	65	35
Totals		
Patients with neurocirculatory asthenia (48)	45	55
Controls (44)	72	28

finger-like, etc. (fig. 1). After much counting and recounting, it was decided that the significant morphologic feature was the simplicity or complexity of the loops, i. e., whether they were (*a*) simple, hairpin forms or (*b*) complex forms, it making no difference whether the complex forms were looped, corkscrewed, spiraled or branched. Thus, only two classes were made in the final counts. When

two or more observations were made on the same patient, the counts were averaged and the average recorded as the score for that patient. The nearest whole number was used, and if the average came out halfway between the two classes, the normal "hairpin" score was given the benefit of the tie. For example, the right hand of one subject showed 5 hairpin forms and 5 complex loops, and the left hand 4 hairpin forms and 6 complex loops in a count of 10. The average was recorded as 5 of each.

RESULTS

From the examination of 48 patients with neurocirculatory asthenia and 44 controls, it was seen that the average percentages of hairpin and complex forms for the patients were approximately equal, whereas the controls had about 7 hairpin forms to 3 complex forms. The data are presented in the accompanying table and in figures 2 and 3.

The table is arranged with two columns, headed "Simple" and "Complex" (fig. 1 *C*). The figures in the first column show the average per cent of simple, hairpin forms found in the various categories listed to the left. For example, the 32 patients with chronic neurocirculatory asthenia had slightly more complex capillary loops than the 16 patients with the acute form, but the difference was too small to be significant.

The controls were of two classes, both of which showed many more simple, hairpin forms than the patients. The first group, called "normal controls," were made up of 13 men—young, vigorous Navy personnel who had been through battle and showed no symptoms. Added to these were 10 soldiers who had finished training but had not been in combat. To get a sample for control who had been living under conditions more like those of the patients with neurocirculatory asthenia, and to see whether chronic illness and convalescence were associated with abnormal capillaries, we examined 21 soldiers with osteomyelitis complicating war wounds in the wards of an Army general hospital. These patients had no neurocirculatory disorder or past history of neurocirculatory asthenia. Among their symptoms were easy fatigability, shakiness, loss of weight, anorexia and nervousness. They also showed more hairpin forms than complex forms. The average for the total control group was 72 per cent hairpin forms and 28 per cent complex forms, whereas the average for the 48 patients with neurocirculatory asthenia was 45 per cent hairpin forms and 55 per cent complex forms. This difference is 8.9 times the standard error of the difference between the two means and is a significant difference, even when corrected for the factor of small numbers.

Figure 2 presents the same data in a scattergram, or spot chart. It brings out the fact that although there is a considerable overlap between the patients with neurocirculatory asthenia and the controls as to per cent of hairpin forms, the averages, as presented in the table, do not distort the facts. This chart shows the results for all our

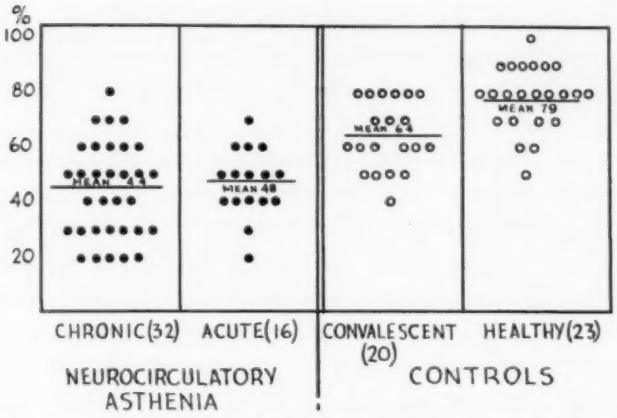


Fig. 2.—Percentage incidence of simple capillary loops in finger nail fold. The data used in the table are here shown on a scattergram. Each dot represents a case, and the ordinates are in percentages of simple capillary loops in each case. Thus, it is obvious that among the controls most subjects had between 64 and 79 simple, hairpin forms, whereas among the patients with neurocirculatory asthenia the greatest percentage falls between 44 and 48. It is also of interest that there is a progressive increase in the number of complex forms when the four classes are taken in sequence: healthy least, convalescent controls next, acute patients with neurocirculatory asthenia next, and patients with chronic neurocirculatory asthenia most.

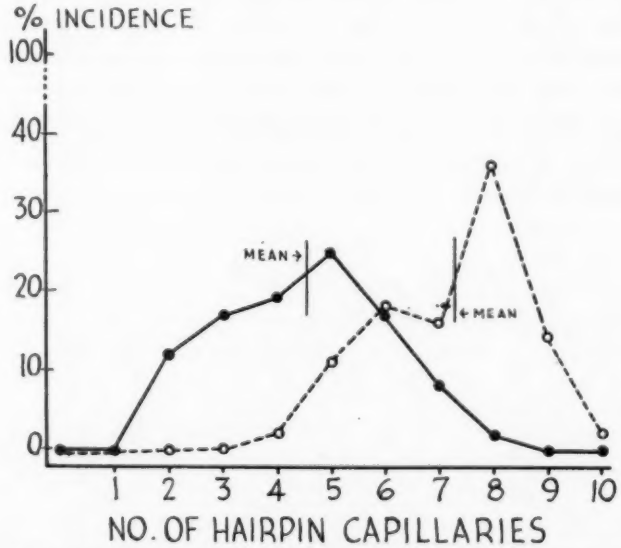


Fig. 3.—Chart showing number of hairpin-shaped capillary loops in 48 patients with neurocirculatory asthenia (solid line and circles) and in 44 controls (broken line and hollow circles). The numbers on the abscissa, from left to right, show hairpin forms divided into classes of 1 out of 10 capillaries, 2 out of 10, and so on, to 10 out of 10, in the last class to the right. The ordinate indicates the percentages of patients and of controls which fell in each of these classes. The data show that the controls had many more hairpin forms and, on the other hand, that the patients with neurocirculatory asthenia had many more twisted and complex forms (see text).

subjects. Moreover, it indicates that there was a consistent progression from most normal to most abnormal, beginning with the normal controls and proceeding through convalescent controls and patients with acute neurocirculatory asthenia to patients with chronic neurocirculatory asthenia.

The contrast between the patients with neurocirculatory asthenia and the controls is given in another way in figure 3, in which the abscissa shows the hairpin forms divided into classes of 1 out of 10 capillaries, 2 out of 10 capillaries, and so on, to 10 out of 10 capillaries. The ordinate shows the percentage incidence of each of these categories.

It will be noted that all the control subjects had at least 4 hairpin forms out of 10 capillaries, whereas 13 per cent of the patients with neurocirculatory asthenia had only 2 out of 10 and 18 per cent had only 3 out of 10. The mean number of hairpin forms per 10 capillaries for the patients with neurocirculatory asthenia is 4.5, whereas the mean for the controls is 7.2. This corresponds with the 45 and 72 per cent shown in the table.

The peak of the curve for the patients with neurocirculatory asthenia is at 5, whereas for the controls it is at 8. In other words, the largest percentage of patients with neurocirculatory asthenia had 5 hairpin forms to 5 complex forms, whereas the largest percentage of controls had 8 hairpin forms to 2 complex capillary loops. In comparing all the normal controls with all the patients, it can be said that the difference betweeen the mean for the two groups is 2.73, and the difference between this difference and the standard error of the difference between the two means is 8.9. The odds against this observation being a chance one are more than $3.9 \text{ by } 10^{11}$ to 1.

COMMENT

The difference in shape of the capillary loops at the edge of the nail fold in patients with neurocirculatory asthenia as compared with that in normal controls is a conspicuous phenomenon. The figures previously cited, which give the standard error of the difference between the two means as 8.9, strongly support the conclusion that this is a significant difference. Nevertheless, the mathematical calculations are reliable only if the original microscopic observations are reliable. It is obvious that there is a subjective element in these observations. The counts are made by observers who might well have a bias and would therefore choose a microscopic field that was more or less normal, thus weighting the data in one way or the other. Such personal equations are impossible to eliminate, but in our opinion they are small and relatively unimportant. In the first place, in the average nail fold, one can find only one or two places where the edge is even enough to give a good sequence of 10 capillaries to count. Second, three observers were employed, and

in some cases two of them checked each other's counts, finding little discrepancy.

Another difficulty is in judging when a capillary has a plain hairpin form and when it is to be considered a looped form. If the area observed shows a thin cuticle at the right angle to the axis of the microscope, the hairpin forms can be observed for a long distance, and eventually many of them are seen to have a twist that could cause them to be classified as "loop" forms. In most cases the capillaries can be clearly seen for only a short distance, so we classified as "loops" of complex form only those capillaries that had the twist near the top, where the arterial limb goes over to the venous (fig. 1 *C*). Such difficulties mean that judgments have to be made and that the subjective element is not negligible.

In the table a comparison of the per cent of hairpin forms and the per cent of complex forms for normal controls and for osteomyelitis controls suggests that there might be a correlation between form of capillaries and convalescence from chronic illness. The difference between these proportions is not great, and the number of subjects is not large. However, a difference of 14 per cent is statistically significant, being 3.5 times the standard error of the difference between the means. The odds against this being a chance observation are about 1,000:1. This suggests that the irregularities found in the capillaries occur in disorders other than neurocirculatory asthenia and that they may be associated with chronic illness or with the convalescent state.

Most authors who have examined these capillaries believe that the variation is "congenital," but they give no proof.[7] Moreover, most of the papers neither define this term nor state their clinical diagnostic terms with enough accuracy to allow valid comparison with their data. Finally, the capillary picture associated with neurocirculatory asthenia somewhat resembles that seen in the nail fold of infants. Some authors, therefore, call these irregular loops embryonic, or primitive forms, but as yet no satisfactory proof has been brought forward that they are not the result of chronic illness. In fact, the data in the table suggest this possibility. We must conclude, therefore, that the question is unsettled and that nothing in our data answers the question as to whether the capillary abnormality is congenital or acquired after birth.

The data show that there is a variation in capillary form that correlates with neurocirculatory asthenia. This observation cannot be used as a specific diagnostic aid, because other investigators have found similar variations with "anxiety neurosis," hysteria and various clinical syndromes accompanied with vasomotor disturbances.[6] It is obvious that

7. Griffith, J. Q., Jr.: Am. J. M. Sc. **101**:439, 1932. Potosky.[3] Paskind and Brown.[5]

more work must be done to prove whether or not the capillary picture can be varied by disease and chronic physiologic disorders. If changes can be produced, one must determine what they are like. Also, the development of the capillary loops must be followed.

SUMMARY

In the nail folds of 48 patients with neurocirculatory asthenia there were significantly more capillaries of complex form than in 44 normal controls. The percentages of complex forms in each class of subjects studied were as follows: normal controls, 21; convalescent controls, 35; patients with acute neurocirculatory asthenia, 53; patients with chronic neurocirculatory asthenia, 56.

The mean number of normal, hairpin-shaped forms for the patients with neurocirculatory asthenia was 4.5 out of 10 capillaries, whereas for the controls it was 7.2 out of 10.

Massachusetts General Hospital (14).

ELECTROMYOGRAPHY IN DIFFERENTIAL DIAGNOSIS OF RUPTURED CERVICAL DISK

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THE presence of fascicular contractions in muscle is a physical sign which is of great help to the clinician in reaching a diagnosis. The electromyograph can be used as a delicate tool for the detection of fasciculations not obvious to the eye, for although in some muscles over which the subcutaneous tissue is thin fasciculations if present can be readily observed, in other muscles even when present they escape observation. In some cases the bilateral or diffuse nature of a lesion can be observed earlier by electromyography than by clinical examination.

The application of electromyography to the detection of fasciculations in muscles due to lesions of the spinal cord and of the peripheral nerves has been in use in this laboratory [1] and in others [2] for some time. In 1944 Hoefer and Guttman [2] described an electromyographic method for determination of the level of lesions in the spinal cord and demonstrated its usefulness in a series of 24 cases of lesion of the cord. Of these cases, 2 were of ruptured cervical disk, the level of which they were able to localize by electromyography to within one or two segments of the actual level, as verified by later operation. These authors suggested that the network of internuncial neurons in the cord may be responsible for the spread of motor unit discharges to segmental levels other than those of the lesion.

In the present study, 10 cases of suspected compression of nerve roots by protruding intervertebral disks have been reviewed in the light of their electromyographic findings. In 9 of these 10 cases, operation

This study was aided by a grant from the National Foundation for Infantile Paralysis, Inc.

From the Electromyographic Laboratory, Department of Psychiatry; the Department of Physical Medicine, and the Department of Surgery, Massachusetts General Hospital.

1. Watkins, A. L., and Brazier, M. A. B.: Studies on Muscle Innervation in Poliomyelitis and Nerve Injuries, Arch. Phys. Med. **26**:69-75 (Feb.) 1945.

2. Hoefer, P. F. A., and Guttman, S. A.: Electromyography as a Method for Determination of Level of Lesions in the Spinal Cord, Arch. Neurol. & Psychiat. **51**:415-422 (May) 1944.

was performed, and therefore confirmation of the segmental involvement was furnished by operative observation, the other case having confirmation by myelographic studies. In 2 cases of suspected ruptured disk with normal electromyograms no lesion of the disk was observed at operation. The electromyographic findings in these cases are also compared with those in cases of anterior horn cell disease in progressive muscular atrophy.

ELECTROMYOGRAPHIC METHOD

The same technic for recording electrical discharges from muscles was used in this work as has been described in previous work from this laboratory.[3] In the routine electromyographic tests on patients coming for clinical diagnosis and localization, surface electrodes have been used. In our experience, little information is lost by the substitution of surface electrodes for needle electrodes, and the ordeal is considerably less for the patient. In some cases of a bilateral lesion of the spinal cord as many as eighteen or twenty pairs of electrodes may be needed for accurate determination of the level of involvement. The advantage to the patient of the surface electrode technic is obvious in such a case. In addition, fasciculations are sometimes not recordable from the first area tested on a muscle, and many shiftings of the electrodes may be needed before the optimum site for recording is found. It is also questionable whether the introduction of the needle electrode into the body of the muscle itself may not set up some irritability and a current of injury, resulting in electrical discharges which are artefacts.

The recording units for this work were both ink-writing oscillographs, one recording from six muscles simultaneously and the other from three. In a few cases a cathode ray oscillograph was used.

RESULTS

For the purpose of analysis of the electromyograms, the cases of protruding intervertebral disk will be reported first.

As examples of the type of examination used and the correlation between clinical signs and electromyographic findings, 2 cases will be presented in some detail, and the other cases in this category will be tabulated later.

Case 1.—The presenting complaints in this case were pain in the neck and left shoulder and arm, with numbness of the middle finger, which was aggravated by coughing, sneezing and straining. There was tenderness over the sixth cervical spinous process. No fasciculations could be seen. Roentgenographic examination with Pantopaque[4] showed a large filling defect at the sixth cervical interspace on the left side. The electromyogram showed multiple spontaneous discharges consisting of clearcut, diphasic spikes occurring in some muscles but not in others.

3. Watkins and Brazier.[1] Schwab, R. S.; Watkins, A. L., and Brazier, M. A. B.: Quantitation of Muscular Function in Cases of Poliomyelitis and Other Motor Nerve Lesions, Arch. Neurol. & Psychiat. **50**:538-545 (Nov.) 1943.

4. An iodized poppyseed oil, with special cohesive properties, used as a contrast medium for myelography.

These discharges were found when the muscles were in complete relaxation. The distribution of these abnormalities may be summarized as follows:

Muscle (Left Side)	Segment		
Deltoid	C5 C6	Electromyogram normal	
Biceps	C5 C6		
Extensor carpi radialis	C6 C7	Area of maximum electromyographic abnormality	Area of electromyographic abnormality (common root C7)
Flexor carpi radialis	(C6) C7 C8		
Triceps	C7 C8 Th1		
Abductor pollicis brevis	C7 C8		
Abductor digiti quinti	C8 Th1	Electromyogram normal	

It will be seen that the abnormal spontaneous discharges occurred only in those muscles served by the seventh cervical root, and therefore one would suspect compression of this nerve root.

Operation revealed a fragment of ruptured disk at the sixth cervical interspace pressing on the seventh cervical root on the left. This was removed and the nerve decompressed. Fifteen days after removal of the fragment electromyographic

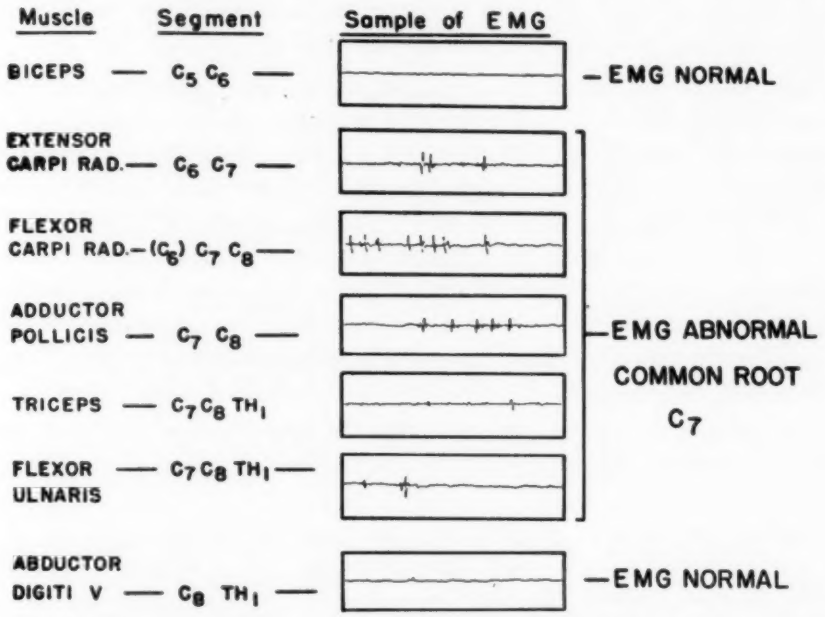
Muscle
Segment
Sample of EMG
BICEPS — C5 C6 —
— EMG NORMAL
EXTENSOR CARPI RAD. — C6 C7 —
FLEXOR CARPI RAD. — (C6) C7 C8 —
ADDUCTOR POLLICIS — C7 C8 —
— EMG ABNORMAL
COMMON ROOT
C7
TRICEPS — C7 C8 TH1
FLEXOR ULNARIS — C7 C8 TH1 —
ABDUCTOR DIGITI V — C8 TH1 —
— EMG NORMAL

Fig. 1.—Electromyograms in a case of ruptured cervical disk. The maximum voltage of the highest discharge is 80 microvolts.

studies were repeated. All trace of spontaneous electrical activity had disappeared, and the only remaining abnormality was some signs of hyperirritability in the left extensor carpi radialis.

Another case is illustrated in figure 1, in which examination with a contrast medium showed a pronounced filling defect at the sixth cervical interspace on the right side consistent with a ruptured intervertebral disk pressing on the seventh cervical root on that side. The details of the case, in brief, are as follows:

CASE 2.—The presenting complaints in this case were severe pain in the right shoulder and arm for two weeks, which was aggravated by coughing and sneezing.

The clinical findings were weakness of the triceps muscle and hyperesthesia of the index finger, tips of the third finger and thumb and the radial aspect of the forearm on the right side. No fasciculations could be seen. Roentgenographic studies with a contrast medium showed a filling defect at the sixth cervical interspace on the right. Although no fasciculations could be detected clinically, many were found electromyographically, with the muscle distribution shown in the following tabulation:

Muscle (Right Side)	Segment	
Biceps	C5 C6	Electromyogram normal
Extensor carpi radialis	C6 C7	Electromyogram abnormal (common root C7)
Flexor carpi radialis	(C6) C7 C8	
Adductor pollicis	C7 C8	
Triceps	C7 C8 Th1	
Flexor ulnaris	C7 C8 Th1	
Abductor digiti quinti	C8 Th1	Electromyogram normal

It will be noticed that of the eight muscles examined, including those of the hand, there were six which were served by some branch of the seventh cervical root. Each one of these six muscles when completely relaxed showed some abnormality in the electromyogram (fig. 1). The two muscles not served by the seventh cervical root gave normal electromyograms.

The rest of this series of cases of ruptured disk is summarized in the accompanying table. In all our cases with positive electromyographic evidence the seventh cervical root was the one compressed. It will be noticed that in a case in which the presence of the lesion was confirmed at operation (case 5) not only those muscles normally innervated by the seventh cervical root were electromyographically abnormal, but the biceps also. Also, in 2 cases (8 and 10) one or two muscles presumably innervated by the seventh cervical root were found to be normal. These anomalies are not surprising, since the actual innervation is not exactly known and the anatomic distribution may vary in different persons.

Of interest in view of these results are the findings in 2 cases in which exploratory laminectomies were done but ruptured disk was not found.

Case 11.—The patient entered the hospital complaining of pain in the left arm and the left side of the neck; this had been present for six months but recently had increased in intensity and was now unbearable. There was no atrophy or paresthesias. Studies of the cervical portion of the spine with a contrast medium showed normal interspaces, although equivocal roentgenographic findings suggested to some observers that compression of the sixth or seventh cervical nerve root might be the cause of the pain. A laminectomy was therefore performed, but no compression of the nerve roots was observed and exploration revealed no abnormality. The final diagnosis was fibrositis due to rheumatoid arthritis.

In this case the electromyogram before operation was also normal. The deltoid, biceps, triceps and extensor and flexor carpi radialis muscles were all normal on the left side, with no spontaneous activity at rest.

Case 12.—The patient complained of pain in the neck and the left arm with some weakness of that arm. There was a history of several accidents. Studies with a contrast medium showed signs suggestive of a lesion at the sixth cervical interspace. A hemilaminectomy was therefore performed on the left, but no pro-

truding intervertebral disk was seen. The electromyogram before operation revealed no abnormalities in any muscle distribution. The subsequent course in this case made it clear that the diagnosis was that of brachial neuritis.

Electromyographic Findings in Cases of Ruptured Cervical Disk

Case No.	Muscles with Abnormal Electromyogram	Muscles with Normal Electromyogram	Localization by Myelogram	Localization by Operation	Compressed Root
1	Extensor carpi radialis C6 C7 Flexor carpi radialis...(C6) C7 C8 Abductor pollicis brevis C7 C8 Triceps.....C7 C8 Th1	Deltoid.... C5 C6 Biceps..... C5 C6 Abductor digiti V... C8 Th1	C6 interspace	C6 disk	C7
2	Extensor carpi radialis C6 C7 Flexor carpi radialis...(C6) C7 C8 Adductor pollicis..... C7 C8 Triceps.....C7 C8 Th1 Flexor ulnaris.....C7 C8 Th1	Biceps..... C5 C6 Abductor digiti V... C8 Th1	C6 interspace	.....	C7
3	Extensor carpi radialis C6 C7 Flexor carpi radialis...(C6) C7 C8 Opponens pollicis..... C7 C8	Trapezius. C1-C4 Deltoid.... C5-C6 Biceps..... C5-C6 Triceps....C7 C8 Th1 Abductor digiti V... C8 Th1	C6 interspace	C6 disk	C7
4	Triceps.....C7 C8 Th1	Deltoid.... ..... Biceps.....	C6 interspace	C6 disk	C7
5	Biceps..... C5 C6 Extensor carpi radialis C6 C7 Triceps.....C7 C8 Th1	Deltoid.... C5 C6	C6 interspace	C6 disk	C7
6	Extensor carpi radialis C6 C7 Triceps.....C7 C8 Th1	Deltoid.... C5 C6 Biceps..... C5 C6 Abductor digiti V... C8 Th1	C6 interspace	C6 disk	V7
7	Triceps.....C7 C8 Th1	Deltoid.... C5 C6 Biceps..... C5 C6	C6 interspace	C6 disk	C7
8	Extensor carpi radialis C6 C7 Flexor carpi radialis...(C6) C7 C8	Trapezius. C1-C4 Deltoid.... C5 C6 Biceps..... C5 C6 Triceps....C7 C8 Th1 Opponens pollicis... C7 C8	C6 interspace	C6 disk	C7
9	Extensor carpi radialis C6 C7 Triceps.....C7 C8 Th1	Trapezius. C1-C4 Deltoid.... C5 C6 Biceps..... C5 C6	C6 interspace	C6 disk	C7
10	Extensor carpi radialis C6 C7 Adductor pollicis..... C7 C8 Triceps.....C7 C8 Th1	Deltoid.... C5 C6 Biceps..... C5 C6 Abductor pollicis brevis.... C7 C8	.....	C6 disk	C7
11	None.....	Deltoid.... C5 C6 Biceps..... C5 C6 Extensor carpi radialis... C6 C7 Flexor carpi radialis... C6 C7 C8 Triceps....C7 C8 Th1	Questionable	None found	None
12	None.....	Deltoid.... C5 C6 Biceps..... C5 C6	Questionable C5	None found	None

COMMENT

To the electromyographer there are certain differences in the recordings obtained from muscles in cases of root compression and those in cases in which there is a degenerative process of the anterior horn cell,

as in progressive muscular atrophy. An electromyogram from 1 of a series of 20 cases of this disease is shown in figure 2. The muscle distribution of abnormalities is, of course, different in these cases because the findings are often bilateral and may occur in the muscles of all four extremities. In the early stage the fasciculations are often not visible to the eye and can be demonstrated only by the electromyograph. Frequently cases are met with in which the only visible fasciculations are in the tongue, but the electromyograph may be able to detect them in the musculature of the trunk and limbs.

Besides the more diffuse distribution of the abnormalities in these cases there are some differences in the pattern of the electrical discharges which are found to be constant. Although less information about the actual electrical event taking place in the muscle can be deduced from surface electrodes than from coaxial needle electrodes, some constantly occurring features are of interest.

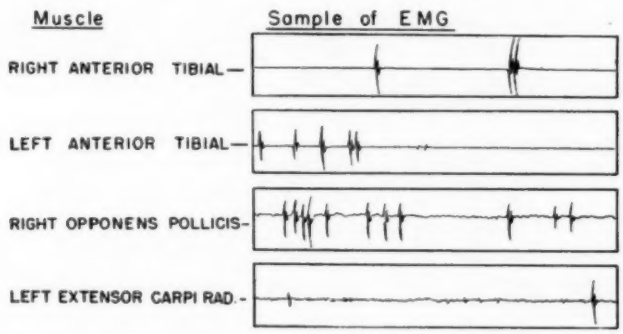

Fig. 2.—Electromyograms in a case of progressive muscular atrophy. The maximum voltage of the highest discharge is 250 microvolts.

In cases of progressive muscular atrophy or amyotrophic lateral sclerosis the voltage is almost invariably higher than in cases of root compression. Voltages of 250 microvolts are commonly met with, whereas in cases of axonal lesions, such as root compression and the neuritides, the discharges rarely reach this level. In the latter cases, however, the discharges from any given muscle tend to be even in voltage, repeating themselves with the same height of excursion. In cases of progressive muscular atrophy, on the other hand, they vary in voltage in a completely unpredictable way; in fact, the outstanding characteristics of these discharges are their irregularity of voltage, of grouping and of rhythm. No set rhythm of discharge is found, and the grouping is so irregular that the spikes may occur singly, or in twos and threes or in multiple groups. The spikes themselves are rather different from those found in cases of root compression, which tend to be almost purely diphasic, with perhaps some repetition of low voltage; but in cases of

progressive muscular atrophy they are usually polyphasic, with one spike of maximal voltage placed in the center of others of lesser voltage.

As has already been mentioned, any explanation of the processes underlying these formations would be pure conjecture, since surface electrodes were used, but some features recur so constantly that conjecture is tempting. For example, the repetitive spikes of lower voltage and even excursion are found in many cases in which an inflammatory or irritative condition of the peripheral axon is present, as in peripheral neuritis; and in these cases of ruptured cervical disk in which electromyographic abnormalities are found it is likely that these discharges are due not so much to impaired conduction as to irritation of the nerve fibers. Grundfest [5] has shown that conduction in nerve fibers is normal even under immense pressure. On the other hand, in cases of progressive muscular atrophy and amyotrophic lateral sclerosis, and of hematomyelia and syringomyelia, in which the anterior horn cell is involved, the repetitive discharges of steady low voltage, so typical of irritation of the peripheral nerve, are rarely found, and if present at all are less persistent.

None of these findings need be confused with the discharges of true fibrillation of denervation, which presumably originate in the sarcolemma. The fibrillations of denervated muscle fibers are of low voltage and short duration (1 to 2 milliseconds) and are not recordable by the ink-writing oscillograph generally used in this work. Their swiftness of phase change necessitates the use of a cathode ray oscillograph. It is for this reason that the term "fasciculations" is specifically used throughout this paper.

The electromyographic details outlined here have proved in practice to be of considerable aid in the differential diagnosis of early anterior horn cell disease and lesions of the spinal root. The present report has laid emphasis on cases of ruptured cervical disk; the clinical diagnosis of these cases has been fully covered by Michelsen and Mixter,[6] who pointed out that the clinical detection and exact distribution of the motor deficit in these cases are indefinite because severe pain interferes with a detailed examination. It is in respect to this problem that the electromyogram takes its place as a diagnostic aid to the localization of ruptured cervical disk. Studies are being made for the application of these methods to the localization of ruptured lumbar disks.

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5. Grundfest, H., in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1936, vol. 4, p. 179.

6. Michelsen, J. J., and Mixter, W. J.: Pain and Disability of Shoulder and Arm Due to Herniation of the Nucleus Pulposus of Cervical Intervertebral Discs of the Lower Cervical Spine, New England J. Med. **231**:279-287 (Aug. 24) 1944.

SUMMARY

The electromyographic findings are reviewed in 10 cases of ruptured cervical disk, in 9 of which operation was performed.

In 2 suspected cases of ruptured disk with normal electromyograms no lesion was observed at operation.

The features of the electromyograms found in cases of irritation of the nerve root by compression are contrasted with those in cases of anterior horn cell disease.

DELIRIUM

IV. Quantitative Electroencephalographic Study of a Case of Acute Arsenical Encephalopathy

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CINCINNATI

IN STUDIES of the effects of anoxia, hypoglycemia and alcohol on the normal electroencephalogram and the correlation of these changes with the degree of reduction of consciousness, we emphasized the fact that the degree of change in frequency in the electroencephalographic record may be of more importance than the appearance of any particular wave frequency.[1] Thus several subjects experiencing comparable reduction in consciousness when exposed on different occasions to anoxia, hypoglycemia and alcohol all showed the same degree of slowing in the electroencephalogram, although the final mean frequency varied widely among the different subjects, depending on the initial mean frequency. With the rather mild disturbance in consciousness induced in these experiments, abnormally slow waves (7 per second or less) appeared only in those instances in which the control records were in the slow normal range. In contrast, the subject with an abnormally fast record (mean frequency, 12.87 cycles per second) had during gross alcoholic intoxication a considerably more "normal" record (mean frequency, 9.72 cycles per second).

In the experiments just cited the effects were acute and of brief duration, and the cerebral disturbance was of mild intensity and of a high degree of reversibility once the noxious factor was removed. It is of both practical and theoretic importance to establish the validity of this principle under conditions more likely to be encountered clinically. In our earlier studies of delirium we were able to follow grossly abnormal electroencephalographic patterns back to normal but never had the

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1. (*a*) Engel, G. L., and Rosenbaum, M.: Delirium: III. Electrocencephalographic Changes Associated with Acute Alcoholic Intoxication, Arch. Neurol. & Psychiat. **53**:44 (Jan.) 1945. (*b*) Engel, G. L.; Webb, J. P., and Ferris, E. B., Jr.: Quantitative Electroencephalographic Studies of Anoxia in Humans: Comparison with Acute Alcoholic Intoxication and Hypoglycemia, J. Clin. Investigation **24**:691 (Sept.) 1945.

opportunity to study the electroencephalogram before the development of the delirium.[2] In the case of acute arsenical encephalopathy here reported electroencephalograms were obtained immediately before and during the acute reaction. This was an incidental observation during a study of the toxicity of Melarsen, a pentavalent arsenical compound (sesquisodium salt of N-(*p*-arsonophenyl)-melamine). This compound contains 20.9 per cent arsenic.[3]

Case 1.—K., a 26 year old married woman, was found to have a positive Wassermann reaction of the blood in May 1943. Six years before she had delivered a 7 month premature child, who had since been found to have congenital syphilis. She received one injection of a bismuth preparation and two intravenous injections of neoarsphenamine at weekly intervals. After the second injection of the arsenical compound a rash developed, which lasted three days. In August 1943 she received one injection of mapharsen, after which she had generalized edema, nausea, and vomiting, but no rash. In November 1943 she was again examined and was found to have positive Wassermann reactions of the blood and cerebrospinal fluid; she was referred to the hospital for therapy.

Physical examination revealed a well developed and well nourished woman with no abnormalities. The neurologic and mental status was normal.

The Wassermann reaction of the blood was positive. The blood and urine were normal. The cerebrospinal fluid was clear and colorless and contained a trace of globulin and 18 white blood cells per cubic millimeter (no differential count was made). The Wassermann reaction was 4 plus and the colloidal gold curve 3355521000. The diagnosis was asymptomatic neurosyphilis.

The patient received 0.5 Gm. of Melarsen intravenously on Dec. 11 and 16, 1943. She complained of nausea and vomited once after the first injection. After the second injection she experienced malaise and a rise in temperature to 100.5 F. On December 20 a third injection was given. After this there developed a pruritic, scarlatiniform rash, most pronounced on the trunk; general malaise; aching in the extremities, with marked muscular tenderness; nausea and frequent emesis; slight generalized edema; generalized lymphadenopathy of a mild degree, and low grade fever (99 to 101 F.). She complained of severe headache and vertigo on movement of the head. Neurologic examination revealed no changes from the previous condition. The patient was drowsy and inattentive, and examination of the mental status revealed evidence of increased fluctuation of the level of awareness.

At the height of the reaction, the urine showed a trace of albumin, with occasional red cells and white cells, and the cerebrospinal fluid contained 72 white cells per cubic millimeter (differential count not made), and a total protein of 110 mg. per hundred cubic centimeters.

Severe symptoms continued for five days and then gradually subsided over the course of ten days. A lumbar puncture repeated six days after the one indicated in the preceding paragraph revealed an initial pressure of 90 mm. of

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2. Romano, J., and Engel, G. L.: Delirium: I. Electroencephalographic Data, Arch. Neurol. & Psychiat. **51**:356 (April) 1944. Engel, G. L., and Romano, J.: Delirium: II. Reversibility of the Electroencephalogram with Experimental Procedures, ibid. **51**:378 (April) 1944.

3. Melarsen was furnished by Parke, Davis & Company, Detroit. This work was done in part under a grant from Parke, Davis & Company.

water, 58 white cells (94 per cent mononuclears) per cubic millimeter and a total protein of 23 mg. per hundred cubic centimeters. All specimens of the spinal fluid gave a positive Wassermann reaction. The patient was seen several months after her discharge from the hospital. There were no abnormal findings, but the serologic reactions of the blood were still positive. Penicillin therapy was recommended to her physician.

Electroencephalographic Studies (figure).—The method of analysis was that previously described.[1b] All analyses were made on the tracing from the left fronto-occipital area.

December 11: Tracings were taken before, during and two hours after the first intravenous injection of 0.5. Gm. of Melarsen. These revealed a fairly regular pattern, with a dominant frequency of 11 to 12 cycles per second and a mean frequency of 11.51 to 11.53 cycles per second. The three records were similar.

December 24: This record was taken at the height of the sensitivity reaction. It revealed a much less regular and a generally slower rhythm, the mean frequency on analysis of the tracing from the fronto-occipital area being 9.12 cycles per second (range, 7 to 12 per second). The slowing was greater in the frontal areas, where occasional 6 per second waves were noted, rarely appearing in bursts.

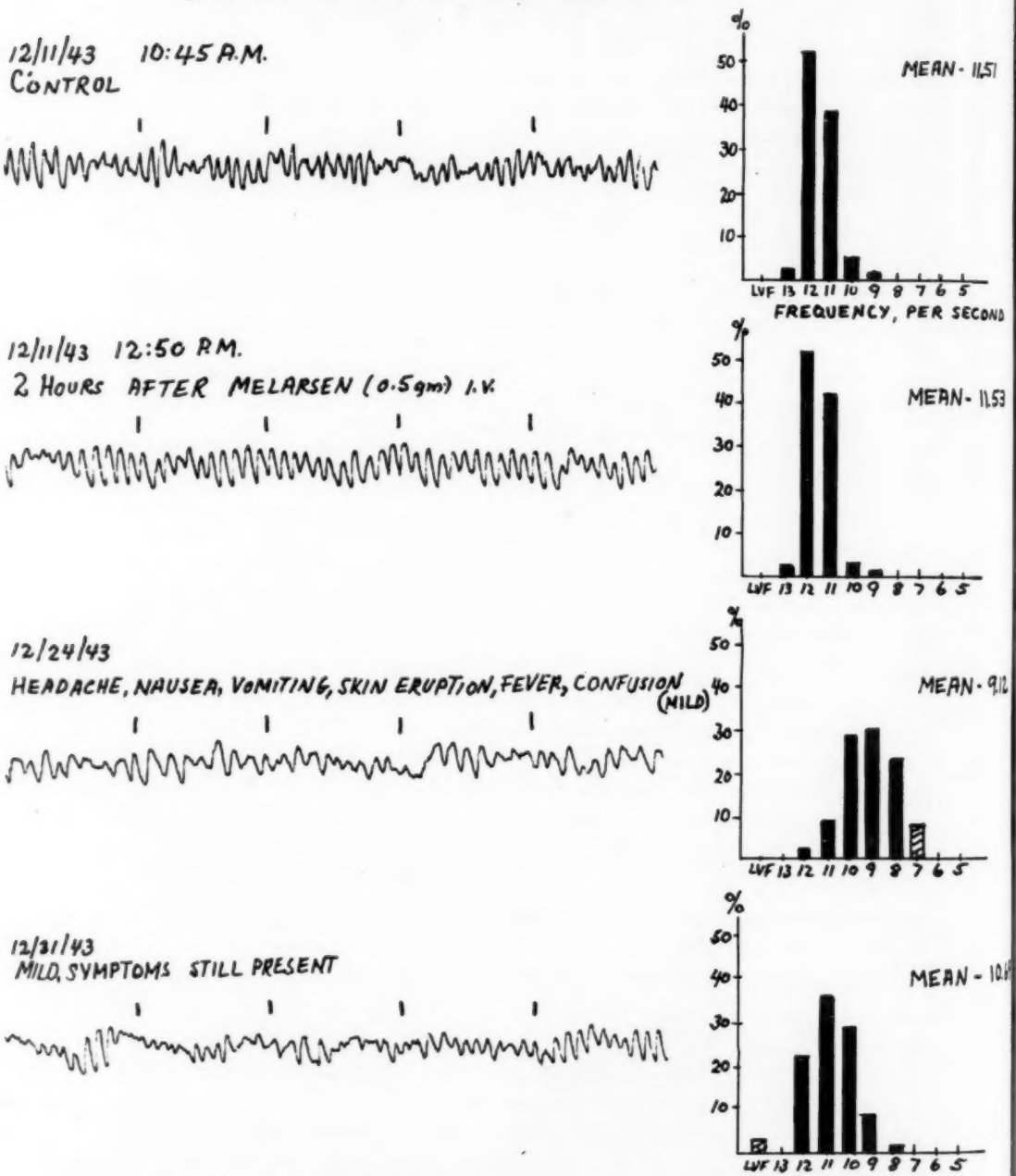
December 31: The patient was recovering but still exhibited mild symptoms. The record showed a more regular and faster rhythm but had not as yet returned to the control pattern. The mean frequency was 10.69 cycles per second.

COMMENT

From the previous history it is apparent that this patient was sensitive to trivalent arsenic. At the initial examination she presented no physical signs or symptoms of active syphilis and was regarded as having asymptomatic neurosyphilis. Examinations of the neurologic and mental status revealed no significant abnormalities. The electroencephalogram taken before treatment was normal, and a record taken during and two hours after the first injection of Melarsen (0.5 Gm. intravenously) revealed no changes, indicating that there was no direct or immediate effect of the drug on the electroencephalogram. The check in the mean frequencies also gives an indication of the reproducibility of the frequency count. Similar studies on 3 other patients also failed to reveal any immediate effect of injections of amounts up to 1 Gm. of Melarsen intravenously.

The reaction began two to three days after the first injection and reached its peak after the third injection. The syndrome, characterized by fever, nausea, vomiting, generalized edema, albuminuria, scarlatiniform eruption, pruritus, myalgia, generalized lymphadenopathy, headache and mild delirium, with increased protein and cells in the cerebrospinal fluid, was of the serum sickness type of drug hypersensitivity.[4] It has not been common for patients to be sensitive to both trivalent and pentavalent organic arsenicals.

4. Longcope, W. T.: Serum Sickness and Analogous Reactions from Certain Drugs, Particularly the Sulfonamides, Medicine **22**:251 (Sept.) 1943.



Electroencephalographic changes during acute arsenical encephalopathy. See text for description.

The magnitude of the pathologic changes in the central nervous system in this case is unknown, but they must have been minor, since the mortality in cases of severe arsenical encephalopathy is high. Roseman and Aring [5] emphasized the essential vascular origin of the pathologic changes in the central nervous system, with the swelling of the vascular endothelium, and often occlusion, of the small vessels. Perivascular necrosis occurs in relation to the alterations in the small vessels. The nonspecific findings of so-called vasoparalysis have also been noted.[6] These vascular lesions are obviously generalized, and not confined to the central nervous system.[4]

In our patient the arsenical medication was discontinued at a time when the reaction was still readily reversible. The diffuse endothelial swelling very likely altered the exchange of gases, substrate and electrolytes between the blood stream and the parenchyma of the brain, leading to interference with cellular metabolism and perhaps to changes in the cell membrane. Products of the local vascular inflammatory reaction, with resultant edema, may also have contributed.

The magnitude of this effect could be estimated by the quantitative change in the mean frequency in the electroencephalogram, which was of the same order as the frequencies observed in our earlier experiments with acute alcoholic intoxication.[1a] The degree of change in consciousness was roughly comparable. It is noteworthy that the electroencephalographic pattern at the time of maximum change would still be considered only in the category of borderline abnormal; yet the change from the control record was considerable. On inspection, the only feature likely to attract attention was the presence of occasional 6 per second waves in the frontal area. There was definite, but not striking, loss of regularity. If a control record had not been available, the significance of this electroencephalographic feature might easily have been overlooked.

Thus, when a "normal" record is obtained on a patient who manifests some disturbance in consciousness of recent and acute origin, it cannot be considered normal for the particular subject until a record is obtained after recovery and some estimate of the degree of change can be made.

SUMMARY

Quantitative electroencephalographic studies were carried out on a patient who manifested an acute reaction to a pentavalent arsenical compound, Melarsen. The patient was known to be sensitive to trivalent arsenic and exhibited a reaction of the serum sickness type, with

5. Roseman, E., and Aring, C. D.: Encephalopathy Following Neoarsphenamine Therapy, New England J. Med. **224**:550 (March 27) 1941.

6. Scheinker, I. M.: Genesis of Encephalopathy Due to Arsphenamine (Central Vasoparalysis Due to Arsphenamine), Arch. Path. **37**:91 (Feb.) 1944.

evidence of mild diffuse encephalopathy. The electroencephalograms obtained before and two hours after the first injection of the arsenical drug were normal and yielded a mean frequency of 11.51 to 11.53 cycles per second. The record at the height of the reaction was only "borderline abnormal." It revealed a slowing in mean frequency to 9.12 cycles per second, but there were only rare waves of a frequency less than 7 per second. This study, again, emphasizes the importance of the degree of change in the electroencephalogram rather than the appearance of any particular wave frequency.

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CHRONIC PSYCHOSES AND ADDICTION TO MORPHINE

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THE PSYCHOSES attributed to the use of morphine may be classified as follows: (1) chronic psychoses due to habitual use; (2) psychoses due to withdrawal, and (3) psychoses due to idiosyncrasy.

At the United States Public Health Service Hospital, Lexington, Ky., which is devoted primarily to the treatment of drug addiction and at which this study was made, there has been little experience with the last type (psychoses due to idiosyncrasy), since the patients are addicts and therefore habitually use large doses of morphine. However, it has been stated that this type of psychosis does occur [1] but is rare and occurs more frequently in women. It is characterized by excitement or delirium. Psychoses due to withdrawal constitute a separate problem.

This study is concerned with an evaluation of the first type, chronic psychoses due to habitual use of morphine. "Psychoses due to opium or its derivatives" is listed in the "Standard Nomenclature of Diseases." [2] These psychoses are described in the "Statistical Manual," published by the National Committee for Mental Hygiene,[3] as "psychotic reactions appearing in the habitual users of opium and particularly its derivative morphine. Such effects appear to show themselves in mental deterioration with demonstrable memory defect as well as ethical and social deterioration."

Von Krafft-Ebing,[4] Edmunds and Gunn,[5] Lambert,[6] Bell [7] and Sandoz [8] all expressed the opinion that the habitual use of morphine

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1. Goodman, L., and Gilman, A.: Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941. Bastedo, W. A.: Materia Medica, Pharmacology and Therapeutics, Philadelphia, W. B. Saunders Company, 1934.

2. Standard Nomenclature of Disease, edited by E. P. Jordan, Chicago, American Medical Association, 1942, p. 100.

3. Statistical Manual for Use of Hospitals for Mental Diseases, ed. 7, New York, The National Committee for Mental Hygiene, 1936.

(Footnotes continued on next page)

causes this type of psychosis. Von Krafft-Ebing [4] stated: "In severe cases we find . . . weakness of memory . . . and occasionally visual hallucination." Edmunds and Gunn [5] wrote: "Eventually melancholia and dementia may follow the long use of opium and especially of morphine." Lambert [6] stated: "Considering the symptoms, memory is one of the faculties first affected and the amnesia is similar to the beginning of senile dementia." On the other hand, many authors have questioned the statement that the habitual use of morphine causes a psychosis. Among these were Dana,[9] Chotzen,[10] Schneider [11] and Kolb.[12] The last-mentioned states:

> . . . Intellectual deterioration is apparently never due to the use of an opiate alone . . . Cocaine is a much more injurious drug, and it seems that most of those who have deteriorated have used both an opiate and cocaine. . . .
>
> There is no destruction of protoplasm such as follows prolonged excessive use of alcohol. Neither nerve cells nor fibers degenerate; consequently the drug cannot produce diseases analogous to Koraskoff's psychosis, acute hallucinosis, or alcoholic multiple neuritis.

If opium and its derivatives cause psychoses, one would expect the incidence of psychoses to be higher among addicts than in a comparable group of nonaddicts. Of approximately 600 male prisoners with addiction to morphine in this institution at the time of writing, 13, or 2 per cent, are classified as psychotic. The average length of sentence for the 600 patients is two and a half years. Using the data of Hobhouse and Brockway,[13] the incidence of psychoses in prisoners with the same average length of sentence who are not addicts would be approximately

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4. von Krafft-Ebing, R.: Textbook of Insanity, Philadelphia, F. A. Davis Co., 1905.

5. Edmunds, C. W., and Gunn, J. A., in Cushny, A. R.: A Textbook of Pharmacology and Therapeutics, Philadelphia, Lea & Febiger, 1936.

6. Lambert, A.: Intoxicants and Narcotics, in Nelson's New Loose-Leaf Medicine, New York, Thos. Nelson & Sons, 1920, vol. 2, p. 555.

7. Bell, M.: Morphinism and Morphinomania, New York M. J. **93**:680, 1911.

8. Sandoz, C. E.: Report on Morphinism to the Municipal Court of Boston, J. Am. Inst. Criminol. **13**:10, 1922.

9. Dana, C. L.: Problems of Drug Addiction, M. Rec. **93**:177, 1918.

10. Chotzen, F.: Zur Kenntnis der Psychosen der Morphiumabstinenz, Allg. Ztschr. f. Psychiat. **63**:786, 1906.

11. Schneider, K.: Zur Frage der chronischen Morphinpsychose und des Zusammenhangs von Sinnestäuschungen und Wahnideen, Ztschr. f. d. ges. Neurol. u. Psychiat. **19**:25, 1913.

12. Kolb, L.: Pleasure and Deterioration from Narcotic Addiction, Ment. Hyg. **9**:699, 1925.

13. Hobhouse, S., and Brockway, A. F.: English Prisons Today, London, Longmans, Green & Co., 1922, pp. 520-529.

2 per cent.[14] This indicates that there is not an increased incidence of psychoses in persons with addiction to morphine.

In an effort to find changes which might be termed characteristic of a morphine psychosis, 19 morphine addicts with chronic psychoses following withdrawal of the drug were examined during the course of one year. They had used morphine habitually; a few had occasionally used dihydromorphinone hydrochloride (Dilaudid), Pantopon (a proprietary preparation containing the total opium alkaloids), opium, diacetylmorphine (heroin) or cocaine. The diagnoses for these 19 patients are given in table 1; they fall into the usual categories. Four patients had an organic type of intellectual deterioration. Two of these men had dementia paralytica; 1 had been chronically alcoholic for forty years, and another's disease was diagnosed as psychosis with cerebral arteriosclerosis.

TABLE 1.—*Chronic Psychoses in Patients Addicted to Morphine.*

		Number of Patients	Average Length of Addiction, Years
Schizophrenia		9	20
Paranoid type	7	..	20
Mixed type	2	..	21
Dementia paralytica		2	23
Psychoses with organic disease of brain		1	31
Psychoses with cerebral arteriosclerosis		1	5
Psychoses with epilepsy and traumatic damage to brain		1	24
Alcoholic deterioration		1	40
Psychoses with mental deficiency		1	14
Psychoses with psychopathic personality		1	12
Paranoid condition		2	14
		19	20

One schizophrenic patient expressed guilt feelings concerning the use of narcotics and other antisocial acts. Accusing voices told him to stop these practices. Another patient with schizophrenia stated that voices asked him in a friendly manner when he was going to stop using morphine. A third patient, given a diagnosis of schizophrenia prior to the use of narcotics, had a persecutory delusional system and auditory hallucinations concerning morphine, narcotic agents and the

14. Hobhouse and Brockway found that the ratio of psychoses to the number of sentences increases with the length of the sentence imposed. In sentences under one month the incidence is less than 0.01 per cent. This rate rises to 0.07 per cent for sentences of three months and continues to increase much more rapidly than the length of the sentence. Prisoners sentenced for one year have a rate of 0.4 per cent; those sentenced for five years, a rate of 3.8 per cent and those sentenced to twenty years, a rate of 24 per cent. With these data, it was determined by interpolation that the incidence of psychoses corresponding to a sentence of 2.5 years would be approximately 2 per cent.

government. In these patients, however, ideas concerning narcotics formed only a small fraction of their total abnormal thought content. It appeared that these ideas were not peculiar to a morphine psychosis but, rather, were incidental to the fact that the existence of these psychotic patients was largely concerned with the procuring and using of narcotics; ideas concerning narcotics were simply woven into typical schizophrenic delusions and hallucinations.

Except for occasional concern with narcotics, as already indicated, the delusions and hallucinations of these 19 patients were not unusual for the diagnoses listed. The general behavior, stream of talk, affect, sensorium and insight were likewise not unusual. Memory defects and deterioration were compatible with these diagnoses. No features peculiar to a morphine psychosis were found.

The Rorschach test was given to 6 men addicted to morphine who had a clinical diagnosis of schizophrenia. Patterns indicative of schizophrenia were found. The records were characterized by extreme variation in form quality of the responses, one of the most reliable signs of schizophrenia. Contamination, which is found in adults only among schizophrenic persons,[15] appeared in 3 of the 6 records. Whole responses increased, together with a decrease in their quality. Confabulatory wholes were present in 2 records. The number of M responses was decreased for all records. The M to C ratio showed a domination of color over movement. All the records were high in CF and C responses, with few, if any, FC responses. Abstract and personal references occurred frequently.

The Rorschach factors correlated with the clinical findings. Failure of the patient's control was shown in the lower percentage of F+ responses or in a high percentage of F responses with a large number of F— responses. Absence of differentiated shading (FK or Fc) also indicated this lack of control. The inability of the schizophrenic patient to handle everyday situations as a result of his lack of contact with reality, together with his futile though ambitious attempts to achieve recognition, was shown in the approach, which was characterized by crude or confabulated wholes and a lack of D responses. Attention to tiny details, representing preoccupation with inconsequential and unimportant things, was found. The lack of human movement responses corresponds to a lack of constructive inner life. Blocking was shown in a rejection of cards and in application of abstract and personal references.

Because it has been stated [3] that in the psychoses due to opium and its derivatives there is a "mental deterioration with a demonstrable memory defect," special attention was given this aspect of the problem.

15. Klopfer, B., and Kelley, D.: The Rorschach Technique, Yonkers-on-Hudson, N. Y., World Book Company, 1942, p. 354.

The Shipley-Hartford Retreat Scale [16] was used in this study for the measurement of intellectual deterioration. This scale consists of a vocabulary test and an abstract thinking test, to be used together. Both are self administering. The vocabulary test is comprised of forty items of the multiple choice type. Each of the items consists of a test word for which the patient must select and underscore from four words the appropriate synonym. The abstract thinking test is comprised of twenty items of the completion type. Each item requires the subject to induce a general principle and deduce a specific answer. The degree of deterioration is expressed as the conceptual quotient. It represents the ratio of the patient's abstract thinking ability to his vocabularly level. Thus, this test makes use of the fact that in mental deterioration vocabulary is relatively preserved, whereas there is a striking loss of abstract, or conceptual, thinking.[17]

Six of the patients with a diagnosis of schizophrenia were given the Shipley-Hartford Retreat Scale and had a median conceptual quotient of 75, indicating some intellectual impairment. However, Shipley and Burlingame [16] found the median conceptual quotient for 96 schizophrenic

TABLE 2.—*Controls and Morphine Addicts Equated for Age and Education.*

	Age, Yr.	Education	Drug History, Yr.
Controls	39.6	11.9	None
Addicts	40.6	11.0	12.7

patients in a state hospital to be 65. When the results for private and state hospital patients were combined, the median conceptual quotient was 75. These results suggest that these 6 psychotic patients with addiction to morphine were not more deteriorated than a group of schizophrenic patients who did not have the addiction.

In a further attempt to evaluate morphine as a cause of mental deterioration, the Shipley-Hartford Retreat Scale was administered to 25 nonpsychotic patients who had been addicted to use of morphine for periods varying from three to twenty years, with a mean of 12.7 years. The results were compared with those for 25 attendants at this institution. The data for these two groups were equated for age and education. The mean age, education and history of drug addicts are shown in table 2. It is noted that the two groups were comparable in age and education.

16. Shipley, W., and Burlingame, C.: A Convenient Self-Administering Scale for Measuring Intellectual Impairment in Psychotics, Am. J. Psychiat. **97**:1313, 1941.

17. Babcock, H.: An Experiment in the Measurement of Mental Deterioration, Arch. Psychol. **18**:105, 1930. Gelb, A., and Goldstein, K.: Psychologische Analysen hirnpathologischer Fälle: Ueber Farbenamnesia nebst Bemerkungen über das Wesen der amnestischen Aphasie, Psychol. Forsch. **6**:127, 1924.

Comparison of the performance of the two groups on the Shipley-Hartford Retreat Scale is shown in table 3.

The ratio of the difference to the probable error of the differences (D : PED) [18] is 1.9. This ratio must be at least 4 to insure significant superiority of one group over another. It is obvious, therefore, that the use of morphine has not increased mental deterioration, as measured by this scale in a group of addicts and compared with the results for a control group equated for age and education. Brown and Partington [19] found no differences between attendants and patients addicted to drugs, using a battery of tests which included the Wechsler-Bellevue test, the Ferguson form boards, the Knox cubes and the Healy Picture completion test.

The addict suffers ethical and social regression; but, as pointed out by Kolb,[12] this is not due to the direct effect of narcotics but, rather, is a result of social consequences of the life of addiction. In most addicts a sufficient amount of a narcotic produces a lethargy and ambition is decreased. Less attention is paid to occupation. Frequently the addict

TABLE 3.—*Scores on Shipley-Hartford Retreat Scale for Controls and Addicts Expressed as the Conceptual Quotient.*

	Mean	Standard Deviation
Controls	85.6	5.2
Addicts	83.6	5.7

stays away from work because of discomfort due to an insufficient amount of the narcotic or because he must look for the drugs. Many addicts associate with criminals in order to continue their supply of drugs. The need for sufficient money to maintain a "habit" frequently leads to stealing. He is held in contempt by others. He fears arrest and incarceration. All these factors lead to ethical and social regression, but intellectual deterioration in the psychologic sense has not been demonstrated.

The following case illustrates many of the pertinent observations of this study.

Paranoid schizophrenia in a patient with drug addiction.

A white man aged 50 was the product of a congenial middle class home, of average economic, social and cultural levels. Except for an excessively close attachment to his mother, no other significant factors in his early development were elicited.

His criminal career dated from at least the age of 19, when he was arrested for petit larceny. His record since that time revealed arrests for shop lifting, automobile theft, grand larceny, robbery, vagrancy and violation of narcotic laws.

18. This measure provides a way of telling whether one group is significantly superior to another group.

19. Brown, R., and Partington, J.: The Intelligence of the Narcotic Drug Addict, J. Gen. Psychol. **26**:175, 1942.

The onset of addiction was in 1914, at the age of 20, by smoking opium, a habit which he continued until 1928, when he began to use diacetylmorphine. He later changed to morphine. Since 1914 he had abstained from drugs for only a few days at a time. Even while incarcerated he was able to obtain narcotics. He gave curiosity and associates as the reasons for first using drugs.

When admitted to this hospital, he did not show signs of physical dependence on narcotic drugs. Physical and neurologic examinations and laboratory tests revealed an essentially normal condition. He was placed in the general hospital population. Approximately eight weeks later he was admitted to the neuropsychiatric ward because of "increasing tension."

He stated that twenty years before he first began to feel the effects of machines that spoke to him about obscene sexual matters. This was ten years after the onset of addiction. This hallucination persisted for two years. It recurred ten years later and continued for several years, and recently these machines had begun to bother him again.

The patient appeared tense and suspicious. He moved his right shoulder in a manneristic fashion, explaining that his arm seemed "hazy" and was coming off. He felt electric currents going through his arm. Occasionally during interviews he stood up and said that the electricity used on him made him feel uncomfortable. He touched the area over his heart, saying that he did this because his heartstrings were broken when his mother died. He occasionally showed blocking, his speech was usually evasive, and frequently he used neologisms. He showed a high degree of tension, and when discussing his delusions he became tearful and asked that no further harm be done to him. Affect was labile and at times inappropriate.

There were elicited loosely organized delusions of persecution. He expressed the belief that the government and particularly the research department at this institution were using various machines and electricity to change his body. He said they put a moving picture machine in his stomach, and in the reflection in his eyes he was able to see the movies. He stated that they had performed an operation on him by means of the radio; they had removed parts of his body and changed its shape. He felt taller than he used to be. At times his ribs seemed hazy to him. He said that his vision had become dimmer and his palate harder. Occasionally he expressed the idea that all this was being done to remove the effects of morphine from his body. However, usually he felt that these experiences resulted from a plan to persecute him. He expressed strong guilt feelings regarding antisocial behavior, including the use of drugs. He heard people over the radio refer to incidents that had occurred to him in the past.

While awake he heard his wife and brother outside his room talking to him about his various troubles, including his present commitment, but he said he was too tired to go out and see them at the time. He was well oriented with respect to time, place and person. General information was good. Calculations were well done. There was no impairment of recent or remote memory. He had no insight.

COMMENT

It is noted that the patients with morphine addiction studied were not using narcotics at the time of examination. It has been observed here that the results of psychometric measurements given while the patient is still using morphine, or soon after withdrawal, are similar to the results obtained for deteriorated patients. This probably accounts for some of the published reports of deterioration in persons with

morphine addiction. Thus, the recent memory defect is temporary and quickly reversible and should not be considered intellectual deterioration, any more than an acutely alcoholic patient would be called deteriorated because of poor recent memory and difficulty in calculating. The persistent delusions and hallucinations exhibited by persons with morphine addiction are explainable on the basis of various organic and functional psychoses, to which morphine addicts, like all people, are susceptible.

An estimation of intellectual deterioration should not be made while the patient is still receiving morphine. In order to eliminate false findings, at least six weeks should elapse after withdrawal of the drug to allow for adequate recovery. One must be certain that the patient has not recently used barbiturates or alcohol. Although the use of alcohol and morphine together is relatively rare, some addicts do use large amounts of both, and the presence of alcoholic deterioration should be considered in such patients. In some cases neurosyphilis accounts for the deterioration.

SUMMARY

1. The incidence of psychoses (2 per cent) among incarcerated persons with morphine addiction was no higher than that (2 per cent) in a comparable group of prisoners without addiction, an observation indicating that the chronic use of morphine is not a cause of psychoses.

2. The psychoses of 19 persons with morphine addiction fell into the usual diagnostic categories. Neurologic and psychiatric examinations failed to reveal anything characteristic of a psychosis due to morphine.

3. Six schizophrenic persons with addiction to morphine were given the Shipley-Hartford Retreat Scale and were found to be no more deteriorated than a control group.

4. Twenty-five nonpsychotic patients with morphine addiction who had used morphine and other narcotics for a mean period of 12.7 years were given the same test and were not found to be deteriorated.

CONCLUSION

The data of this study indicate that the habitual use of morphine does not cause a chronic psychosis or an organic type of intellectual deterioration.

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BROMINE CONTENT OF THE BLOOD IN MENTAL DISEASES

II. Manic-Depressive Psychosis

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IN A previous paper,[1] a survey of the literature dealing with blood bromides in mental diseases was presented. Several investigators [2] have made blood bromide studies of patients with manic-depressive psychosis. Zondek and Bier,[2a] in 1931, reported that in 29 out of 34 cases of manic-depressive psychosis studied the blood bromine content was from 40 to 60 per cent below the normal value (1 mg. per hundred cubic centimeters) established by them. These investigators obtained an average value of 0.572 mg. per hundred cubic centimeters for the 34 cases but did not state whether the patients were in the manic or in the depressed stage. Sacristán and Peraita [2b] analyzed the blood of 13 women classified as manic, hypomanic or melancholic and obtained bromine values ranging from 0.161 to 0.684 mg. per hundred cubic centimeters, with an average value of 0.423 mg. All these values were lower than the normal values obtained by the same method. Hennelly and Yates,[2c] using a new and more accurate analysis of their own, examined the blood of 7 male patients with manic-depressive insanity. They reported that the bromine content was low in 5 patients

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The present investigation was made possible through the courtesy of the staff of the Columbus State Hospital for the Insane, Dr. J. F. Bateman, Superintendent. Drs. Rothermich, Michael and Whittenbrook, selected the patients and furnished the diagnosis for this study.

1. Wikoff, H. L.; Martin, R. L., and Marvin, T. R.: Bromine Content of the Blood in Mental Diseases: I. Dementia Precox, Arch. Neurol. & Psychiat. **53**:305 (April) 1945.

2. (*a*) Zondek., H., and Bier, A.: Brom im Blute bei manisch-depressivem Irresein, Biochem. Ztschr. **241**:491, 1931. (*b*) Sacristán, J. M., and Peraita, M.: Ueber den Bromspiegel des Blutes bei manisch-depressivem Irresein, Klin. Wchnschr. **12**:469, 1933. (*c*) Hennelly, T. J., and Yates, E. D.: Blood Bromine in the Psychoses, J. Ment. Sc. **81**:173, 1935. (*d*) Meier, C. A., and Schlientz, W.: Neuere Untersuchungen über den Bromspiegel im Blut bei Psychosen, Klin. Wchnschr. **15**:1845, 1936. (*e*) Chatagon, P., and Chatagon, C.: Le métabolism du brome dans l'organisme humain, Compt. rend. Acad. d. sc. **202**:1119, 1936.

but stated that there was no correlation between the bromine content of the blood and the phase of the psychosis. Meier and Schlientz,[2d] studying the bromide content of the blood of patients with psychoses, included 10 patients with manic-depressive psychosis. Four of these patients were in the manic phase and 6 in the depressive phase. Later, when 1 of the patients previously in the manic phase entered the depressive phase, his blood bromides were redetermined. These authors stated that the blood bromides were low in patients with manic-depressive psychosis, an observation confirmed in all but 2 of their cases. Pierre and Camille Chatagon [2e] found that the blood bromine values were higher than normal in 23 out of 31 cases of manic-depressive psychosis which they had studied.

Because the results obtained by previous investigators were not in agreement, and because the total number of cases reported by any of these workers was relatively small, an extensive study of the blood bromide content of patients with manic-depressive psychosis was made.

The subjects chosen had all been inmates of the Columbus State Hospital for the Insane for more than three months, and some had been in residence there for more than ten years.

The method of bromide analysis previously devised by one of us (H. L. W.) [3] was used for this investigation. The accompanying table gives the results for 116 patients with manic-depressive psychosis. In 5 instances the same patients were reexamined at a later date. Eighty-three (68.6 per cent) of the determinations were made while the patients were in the stage of remission; 27 (20.3 per cent), while in the manic stage, and 11 (9.1 per cent), while in the depressive stage.

Since in the majority of the patients the condition was in a stage of remission when samples of blood were drawn, the general average for bromine (0.459 mg. per hundred cubic centimeters of whole blood) for all the patients was greatly influenced by this group. Sixty of the 83 subjects in the remission stage (72.4 per cent) had less than 0.459 mg. of bromine per hundred cubic centimeters of whole blood, while only 70 of the entire series of 116 subjects, or 60.3 per cent (72 of 121 determinations, or 59.5 per cent), had less than the average amount (0.459 mg.). Although the bromine content for all subjects ranged from 0.08 to 2.66 mg. per hundred cubic centimeters of blood, actually there were only 7 whose bromine value exceeded 1 mg. per hundred cubic centimeters.

The 83 subjects in the remission stage had an average of 0.349 mg. of bromine per hundred cubic centimeters of blood, with 50 (60.5 per cent) of them having less than the average amount of bromine. The individual amounts ranged from 0.08 to 0.90 mg. per hundred cubic centimeters.

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3. Wikoff, H. L.; Bame, E., and Brandt, M.: A Method for the Determination of Bromide in a Protein-Free Filtrate, J. Lab. & Clin. Med. **24**:427, 1939

The limited number of patients in the manic and in the depressive stage does not seem to warrant conclusions for these groups at this time. However, it may be noted that the average bromine values for the patients in these two groups, 0.728 and 0.629 mg., respectively, were lower than the average value (0.81 mg. of bromine per hundred

Bromine Content of Blood of Patients with Manic-Depressive Psychoses

Remission Stage						Manic Stage			Depressive Stage		
Case No.	Age	Bromine, Mg./100 Cc. Whole Blood	Case No.	Age	Bromine, Mg./100 Cc. Whole Blood	Case No.	Age	Bromine, Mg./100 Cc. Whole Blood	Case No.	Age	Bromine, Mg./100 Cc. Whole Blood
Males			Females			Males			Males		
1	50	0.32	44	54	0.18	84	68	0.40	108	48	0.92
2	55	0.57	45	60	0.40	85	72	0.50	109	60	0.45
3	72	0.48	46	88	0.14	86	51	0.47	110	57	0.80
4	60	0.50	47	73	0.13	15*	46	0.49	111	58	0.34
5	68	0.36	48	71	0.12	87	55	0.55	23*	40	0.36
6	65	0.32	49	55	0.16	88	60	0.60	112	69	0.64
7	..	0.40	50	55	0.15	89	44	0.75			
8	46	0.90	51	66	0.20	89*	45	0.64	Females		
9	63	0.73	52	56	0.11	90	68	2.66 (restrained)	113	72	0.94
10	66	0.67	53	53	0.19	90*	69	0.54 (not restrained)	114	42	0.76
11	63	0.34	54	40	0.32				115	58	0.94
12	47	0.45	55	52	0.48	91	68	0.71	102*	38	0.22
13	54	0.35	56	60	0.67	92	54	0.50	116	46	0.55
14	67	0.41	57	58	0.13	93	63	0.13			
15*	45	0.67	58	52	0.27						
16	69	0.23	59	70	0.38						
17	56	0.21	60	42	0.34	Females					
18	33	0.49	61	64	0.17						
19	81	0.22	62	54	0.31	94	68	0.50			
20	71	0.62	63	61	0.41	95	68	0.98			
21	36	0.49	64	62	0.25	96	61	0.38			
22	55	0.10	65	56	0.17	97	77	0.77			
23*	41	0.77	66	40	0.08	98	40	0.32			
24	..	0.27	67	55	0.19	99	47	0.42			
25	48	0.59	68	47	0.32	100	52	0.94			
26	68	0.20	69	52	0.36	101	53	1.11			
27	68	0.59	70	46	0.30	102*	38	1.34			
28	68	0.13	71	41	0.17	103	59	0.45			
29	49	0.52	72	57	0.39	104	35	0.41			
30	57	0.80	73	45	0.28	105	48	1.90			
31	32	0.50	74	57	0.13	106	58	0.81			
32	63	0.37	75	52	0.25	107	57	0.39			
33	37	0.67	76	..	0.21						
34	40	0.78	77	57	0.24						
35	55	0.62	78	32	0.17						
36	54	0.59	79	56	0.19						
37	56	0.29	80	53	0.09						
38	65	0.40	81	48	0.23						
39	..	0.12	82	46	0.32						
40	61	0.18	83	54	0.15						
41	41	0.33									
42	67	1.13									
43	76	0.50									

* The asterisk indicates that two determinations were made.

cubic centimeters of blood) previously determined [4] for normal healthy persons residing in Columbus. Eighty per cent of the blood bromine values for the normal subjects differed from the average value by less than 0.2 mg. per hundred cubic centimeters, but only 50.8 per cent of the values for the manic-depressive group were within 0.02

4. Wikoff, H. L.; Brunner, R. A., and Allison, H. W.: The Normal Bromine Content of the Blood of Healthy Individuals, Am. J. Clin. Path. **10**:234, 1940.

mg. of the average value. While the subjects with dementia precox previously studied [1] also had less bromine in the blood than the normal persons, 80 per cent of them had blood bromine values differing from the average amount by less than 0.02 mg. per hundred cubic centimeters.

SUMMARY

Of the 116 patients in this series, 83 were in the stage of remission. The average bromine content of the blood of these 83 patients was found to be 0.349 mg. per hundred cubic centimeters. This value is considerably lower than the average (0.81 mg. per hundred cubic centimeters of blood) obtained by the same method for normal persons residing in the same city.

Twenty-seven patients in the manic stage had an average blood bromine content of 0.728 mg. per hundred cubic centimeters. Eleven patients in the depressive stage had an average blood bromine content of 0.629 mg. per hundred cubic centimeters.

For both the manic and the depressive patients, the average value for blood bromine was appreciably higher than the average for patients in the remission stage. However, the average for each group, in manic and depressive stages and in remission, is below that for normal persons living in the same city.

In only 10 of the entire series of 116 patients was the amount of bromine in the blood above the average found for normal persons.

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CEREBRAL DYSRHYTHMIA AND PSYCHOPATHIC PERSONALITIES

A Study of Ninety-Six Consecutive Cases in a Military Hospital

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RECENT communications report a high proportion of electroencephalographic abnormalities among persons with behavior disorders (Hill and Watterson,[1] Silverman,[2] Knott and Gottlieb [3] and Silverman and Rosanoff [4]). Their findings suggest that organic factors should be weighed more heavily in considering the etiology of psychopathic states.

The chief psychiatric connotations of psychopathy are widely understood. Cleckley,[5] Darling [6] and others have suggested that the condition arises from a defective development of the superego, and constitutional factors have been emphasized by Henderson [7] and others. For our purpose, it appeared unwise to deviate from the view that the diagnosis "constitutional psychopathic state" should be made only when the longitudinal study of the patient's personality presents sufficient evidence for the formulation of a valid psychodynamic interpretation of that entity. However, partial manifestations of the psychopathic character, often considered as identical with the condition per se, may occur in

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1. Hill, D., and Watterson, D.: Electroencephalographic Studies of Psychopathic Personalities, J. Neurol. & Psychiat. **5**:47-65, 1942.

2. Silverman, D.: Clinical and Electroencephalographic Studies on Criminal Psychopaths, Arch. Neurol. & Psychiat. **50**:18-33 (July) 1943.

3. Knott, J. R., and Gottlieb, J. S.: Electroencephalographic Evaluation of Psychopathic Personality, Arch. Neurol. & Psychiat. **52**:515-519 (Dec.) 1944; Electroencephalograms in Psychopathic Personalities, Psychosom. Med. **5**:139-141, 1943.

4. Silverman, D., and Rosanoff, W. R.: Electroencephalographic and Neurologic Studies of Homosexuals, J. Nerv. & Ment. Dis. **101**:311-321, 1945.

5. Cleckley, H.: The Mask of Sanity, St. Louis, C. V. Mosby Company, 1941.

6. Darling, H. F.: Definition of Psychopathic Personality, J. Nerv. & Ment. Dis. **101**:121-126, 1945.

7. Henderson, D. K.: Psychopathic States, New York, W. W. Norton & Company, Inc., 1939.

post-traumatic conditions or as sequelae of encephalitis, or they may accompany the progressive disorganization of activity of the frontal lobes due to cerebral tumor. Congenital syphilis, complications of pertussis referable to the central nervous system and other disturbances having their origin in infancy may also play a role in its development, and certain disorders in which episodic aggressive activity is a salient feature are thought to be allied to the epileptic states (Henderson [7]). While it cannot be presumed that every case of such a disorder will be eliminated from the constitutional psychopathic group on the basis of the psychiatric formulation, the etiology of the organic variants becomes clear when a cleavage from the pattern of a hitherto normal personality occurs as an aftermath of a neurologic condition.

By electroencephalographic recording there is hope of identifying certain cases in which, though the neurologic evidence of involvement may be obscure, the organic contribution to the causation of psychopathy may be large. However, it is known that abnormal records do occur in normal control groups, and in the absence of specific criteria of abnormality, such as the records of paroxysmal activity (Gibbs [8]) offer in cases of epilepsy, judgment concerning the clinical significance of an abnormal electroencephalographic record in the diagnosis of a psychopathic disorder must have its basis in statistical comparisons.

The incidence of so-called electroencephalographic abnormalities in normal population groups has varied from 5 to 20 per cent in different studies. Such differences may be explained by variations in the rigidity with which the biologic criteria of normality are applied and the vagaries in classification of records, which may cause certain borderline findings to be interpreted as normal in one series and as abnormal in another. Particularly in the interpretation of records containing slow sequences, the amplitude of the slow waves may be the deciding factor in placing a record in a normal or in an abnormal category.

The occurrence of high percentages of electroencephalographic abnormalities in series of psychopathic subjects already reported in the literature dictates the need for further studies of groups selected in different situations. Our study was undertaken to provide data concerning the incidence of electroencephalographic abnormalities in persons with constitutional psychopathic states diagnosed in a military hospital. In a large series of these patients the severer manifestations are the rule, since milder personality maladjustments are usually studied in outpatient clinics; also, the diversity of symptoms is sufficient to make the group representative of the total concept of psychopathy postulated by numerous investigators.

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8. Gibbs, F. A.: Electro-encephalography, in Solomon, H. C., and Yakovlev, P. I.: Manual of Military Neuropsychiatry, Philadelphia, W. B. Saunders Company, 1944.

Every effort was made to secure a nonselected group and to achieve accurate diagnostic consideration in each case. The patients were taken in consecutive order for electroencephalographic study after they had appeared before a formal hospital board of three experienced psychiatrists, all section chiefs in a specialized military neuropsychiatric hospital. Complete medical, neurologic, laboratory and, where indicated, roentgenologic studies were made to rule out coexisting organic disease before the patients were brought before the board. Various lengths of service were represented in the group; enlisted women as well as men were included, and a variety of manifestations of psychopathy in different degrees of severity were represented. When it was evident that a suitably extensive trial at duty had not been given to assure opportunity to adjust, the patient was returned to duty with recommendation for further trial. The series included 96 patients. Clinical data were also available on 8 other patients who appeared before the hospital boards during the period in which the study was being conducted.

PSYCHIATRIC EVALUATION OF CASE MATERIAL

In all cases included the diagnosis of constitutional psychopathic state was made in accordance with the military terminology during the period selected for the survey. In the case study, the severity of each of a variety of manifestations of psychopathy was assessed for the purpose of establishing correlations between the gravity of the symptoms and the type of electroencephalographic record. The manifestations included in this survey were inadequacy, emotional instability, aggression, overt asocial behavior in the premilitary and in the military situations, absence without leave, alcoholism, drug addiction, sexual psychopathy and fabrication. The coexistence of psychosomatic complaints and of organic illness was also considered. There were 96 men and 8 women. The ages ranged from 18 to 42 years. Approximately 45 per cent of the total series were between the ages of 21 and 26 years. Total durations of service varied from five months to four and one-half years, and there was an approximately even distribution of subjects with periods of service between twelve and thirty-six months. Twelve of the men were military prisoners at the time of admission to the hospital. A brief summary of the salient psychiatric data follows:

Inadequacy.—Mild manifestations were defined to include marginal social and economic adjustment in premilitary life, lesser degrees of nomadism, frequent lack of or change in employment, and truancy and other behavior difficulties during childhood. In the intermediate grade of inadequacy, in addition to some or all of the aforementioned manifestations, were repeated minor infractions of the law, marital difficulties and definite evidence of military maladjustment. The severest form

of inadequacy was characterized by petty thievery of frequent occurrence, conviction for criminal offenses or serious military insubordination. Approximately 25 per cent of the total number of patients showed severe inadequacy, and 6 of the 12 military prisoners were in this group. Another 50 per cent of the total series gave evidence of inadequacy of intermediate severity. There appeared to be a high correlation between the severity of manifestations of inadequacy in premilitary life and the frequency of absences without leave that occurred during military service.

Emotional Instability.—Twenty-five per cent of the patients had a history of one or more suicidal attempts in response to frustration or as an effort to relieve a situation regarded as intolerable. These personalities were assessed as displaying emotional instability of the severest degree, as were 2 others with a history of self mutilation. One of the latter admitted intent to avoid hazardous duty. A history of mood depressions with the existence of manifestations of lesser severity was the basis for assessing instability of intermediate severity, and 30 per cent of the total number belonged in this category. The rest had manifestations of lesser severity.

Aggression.—Twenty per cent of the total series did not manifest aggressive tendencies; an additional 40 per cent showed aggression as a subdominant characteristic. Overt hostility, frequent fights and marital quarrelsomeness of marked degree were manifested by 35 per cent. One member of the series showed episodic uncontrolled aggression, homicidal in character, and 4 others manifested it to a degree that could be considered either as homicidal in intent or as necessitating criminal action.

Overt Asocial Behavior.—Seventy per cent of the series gave no concrete evidence of overt asocial behavior during the premilitary period. Of the remainder, 9 had a substantiated history of one or more arrests or confinements of minor character, and 10 had at least one reformatory or prison sentence in the premilitary record with additional evidence of criminal tendencies. There were no confirmed criminals in the group. In evaluating the military evidence, only military records substantiating the occurrence of thievery or other asocial trends were considered; and absence without leave and minor evidences of insubordination of debatable value in indicating criminal tendencies were eliminated. Sixteen per cent had one military conviction, and the offenses of 2 others were graded as more serious, for the offense was a repetition of one for which a conviction had been secured previously in civilian life.

Absence Without Leave.—Forty-six per cent of the men had no significant history of such absences, and none of the women had committed the offense. A small percentage of the men had fewer than

four offenses, and approximately 40 per cent had four or more. The remaining 10 per cent had had one or more absences of such long duration as to indicate that the offense represented the severest manifestation in this regard.

Alcoholism.—One third of the total number showed some evidence of alcoholism, and of these, 20 had been described in prior clinical records as "chronically alcoholic." These 20 subjects gave abundant civilian and military evidence of the use of alcohol; the other alcoholic patients had lesser manifestations. None of our subjects gave evidence of the performance of definitely asocial acts while under the influence of alcohol.

Addiction to Drugs.—This was not a common finding in the present series. Seven patients indicated that they smoked marihuana cigarets; another 7 gave a history of having at one time or another experimented with the use of more conclusively habit-forming drugs.

Sexual Psychopathy.—Twelve of the men gave a history of sexual psychopathy, but only 2 could be regarded as overtly homosexual. The remainder had controlled their homosexuality, participating intermittently either because of lack of heterosexual outlets or for financial gain. One exhibited perversion in heterosexual relationships.

Medical History.—Evidence of organic disease as a cause of admission to the hospital played an unimportant role in this series. Seven men were admitted to the hospital for psychosomatic complaints, however; and an additional 8 patients, who were admitted because of consistent failure to adjust to the military situation, complained of psychosomatic symptoms after admission. Five patients had a history of head injury, but no neurologic sequelae were present. In no case did encephalitis or any manifestation of childhood disease that might be expected to cause the development of psychopathic character appear to be a contributory factor.

ELECTROENCEPHALOGRAPHIC RESULTS

A standard eight lead electroencephalographic record, recommended by the Office of the Surgeon General, United States Army, and its electroencephalographic consultant, Dr. F. A. Gibbs, was taken in each case. Studies were repeated when the initial recording did not provide satisfactory results. Eight of the total series of 104 recordings were eliminated from consideration because artefacts made the results unsatisfactory. Recording was usually done at an amplification of 8 mm. per 50 microvolts. Care was taken not to filter the faster frequencies excessively, so that this type of activity would not be eliminated from the records. A twenty minute record, including combinations of all leads and two minutes each of hyperventilation and posthyperventilation, was routinely used.

With qualifications to be specified, the Gibbs [8] criteria for classification of records were followed. All records containing 8½ to 12 per second frequency and those showing low voltage activity were classified in a single "normal" group.

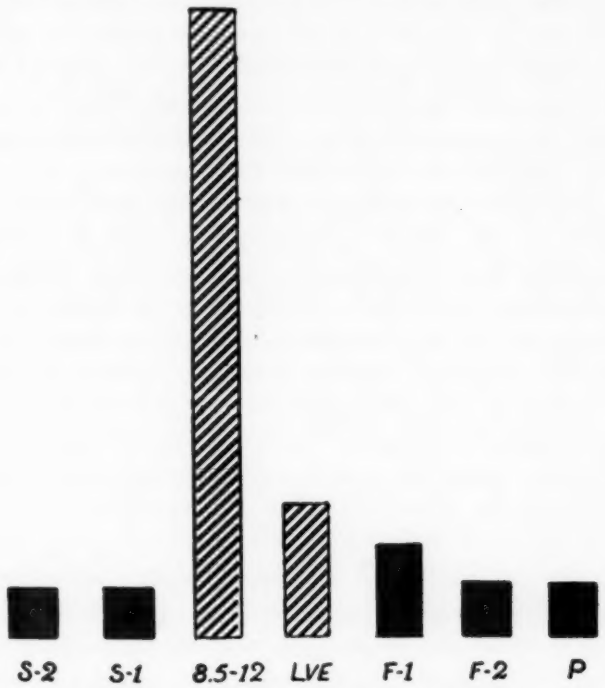
Particular care was taken in classifying the records with borderline slow (S-1) activity, the following statement by Gibbs being taken as the basis for distinguishing between the S-1 and the 8½ to 9 per second frequencies: "Moderate amount of activity slower than 8½ per second in any lead. Amount is considered in terms of amplitude and frequency of the slow activity, percentage of time present, and the number of leads in which it appears." We arbitrarily established 35 microvolts as the criterion of amplitude for slow sequences in this study, and slow activity of lesser amplitude was consistently interpreted as low voltage. Also by arbitrary definition we classified records showing the F-1 and S-1 frequencies of the Gibbs classification as borderline abnormal and the records with the F-2, S-2 and paroxysmal activities as abnormal. The term paroxysmal activity was more broadly interpreted than is the usual practice under the Gibbs classification and was made to include slow dysrhythmias of paroxysmal character. These were mentioned by Jasper[9] (Penfield and Erickson, page 403).

Of the 96 records, 72 per cent fell within the normal range (figure). This included all the records of 8½ to 12 per second frequency and of low voltage activity. The 61 per cent of the total which constituted the records of 8½ to 12 per cent frequency was made up of 32.6 per cent which were quite regular in amplitude and frequency, 13.7 per cent showing mild irregularity of amplitude and 14.7 per cent showing mild irregularity of frequency. Records of borderline abnormality, the S-1 and F-1 categories, comprised 12.6 per cent of the total. This included 4.2 per cent with S-1 activity and 8.4 per cent of F-1 activity. The percentage of records of the S-1 type would have been increased had several of the records with paroxysmal sequences of slow activity been classified in the S-1 category rather in the category of paroxysmal activity. Abnormal records of the F-2 and S-2 type made up 9.4 per cent of the total of our series; 4.2 per cent were of the S-2 variety, as compared with 0.7 per cent in Gibbs's control series, and 5.2 per cent were of the F-2 type, as compared with 0.4 per cent of Gibbs's controls. Abnormal records with paroxysmal activity represented 5.2 per cent of our total series; but, as previously indicated, this figure included "paroxysmal slow dysrhythmias" and therefore could not be compared reliably with Gibbs's controls. Five records showed some degree of build-up on hyperventilation. Two of these were classified with the normal records because the build-up was not significant and the records were not otherwise abnormal. For other reasons, 2 other records with build-up were classified as in the paroxysmal and 1 in the F-2 category.

The records were also studied with a view to determining whether or not an increased incidence of abnormality in the electroencephalograms was associated with the various manifestations of psychopathy of the severest degree. Certainly, there was no tangible evidence that

9. Jasper, H. H.: Electroencephalography, in Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C Thomas, Publisher, 1941.

this was the case. Of 25 patients rated as presenting the severest manifestations of inadequacy, 5 showed abnormal records, 3 of these being of the F-2 and 1 of the paroxysmal type. In addition, 2 of this group had records of borderline (F-1) type. Of 37 patients manifesting less severe grades of inadequacy, 2 had records of paroxysmal activity, and 2 records of F-2 type. The 23 patients who showed the severest emotional instability included 3 who had abnormal records (2 with the F-2 type and 1 with the paroxysmal type) and 3 who had borderline abnormal (F-1) records. Of 44 subjects manifesting the



Histogram indicating the distribution of electroencephalographic frequencies for 96 records in terms of the Gibbs classification. Slow dysrhythmias of paroxysmal character are included with the paroxysmal type. Diagonal lines indicate the distribution of records conventionally designated as normal; black indicates the distribution usually regarded as abnormal. All records were obtained from patients with disorders diagnosed as a constitutional psychopathic state.

Analysis of the record showed that 72.5 per cent fell in the normal range (61 per cent in the 8½ to 12 per second category and 11.5 per cent in the low voltage category), 12.6 per cent were borderline abnormal (4.2 per cent in the S-1 category and 8.4 per cent in the F-1 category), 14.6 per cent were abnormal (4.2 per cent in the S-2 category, 5.2 per cent in the F-2 category and 5.2 per cent in the paroxysmal category) and 5.2 per cent showed a build-up response on hyperventilation.

lesser degrees of emotional instability, 4 had abnormal records, including 3 with the paroxysmal and 1 with the S-2 type. With respect to manifestations of aggression, overt asocial behavior, absence without leave, alcoholism, drug addiction and homosexuality, there was no difference

in the incidence of abnormality between patients with negative and those with positive histories. In the group of 12 prisoners, 2 had records with paroxysmal activity, and 2 had records of the F-2 type; however, the number of prisoners was too small to render the apparently larger incidence of abnormality significant as compared with that for the non-prisoner group.

The over-all survey of our material shows a somewhat higher incidence of electroencephalographic abnormality in this series of 96 patients with psychopathic states diagnosed in the military setting than in normal controls reported in the literature. However, our percentage of abnormality is low as compared with that for other recently reported series of psychopathic subjects. In small part, this may be due to rigid criteria employed in designating a record as abnormal, a conservatism which we believe to be justifiable in view of the present lack of electrophysiologic standards for assessing the variations of the normal. Otherwise this series of subjects selected by psychiatric criteria as constitutionally psychopathic is not notably set apart from normal standards by electroencephalographic abnormality. Whereas specific exception can be made to this interpretation so far as the relatively higher incidence of records containing S-2, F-2 and paroxysmal activity is concerned (as compared with the over-all incidence of abnormality), it is our view that further extension of knowledge in the field of electronic recording may lead eventually to the elimination of subjects presenting such records from the category of the constitutional psychopathic state.

COMMENT

Whereas the present study of persons with a disorder diagnosed as constitutional psychopathic state in the military setting shows a somewhat higher incidence of abnormal records than would be expected in a corresponding group of normal controls, it was not sufficiently high to indicate that the usual psychiatric criteria carefully applied are ineffective in screening out the cases with strong organic determinants. The diagnostic criteria used in the selection of subjects were based on the evaluation of the total personality, indicating in the longitudinal history of the patient a continuous projection of hostility onto the environment. Search of the history for manifestations of the symptoms most frequently associated with psychopathy was regarded as the marshaling of evidence to support the diagnosis in a particular case. The well known fact that some, even all, of these symptoms might develop as an aftermath of infection of the central nervous system or of trauma, and that undisputed infantile or adolescent involvement may appear to influence the subsequent development of psychopathic character, leads us to recommend, however, that those patients who show definite

electroencephalographic abnormality be reexamined with a view to excluding a possible organic cause.

It might be expected that a correlation between the symptoms of psychopathy and electroencephalographic abnormality would become apparent in a higher incidence of abnormal records for persons showing severe as compared with mild manifestations. A series of manifestations, including inadequacy, emotional instability, aggression, homosexuality, alcoholism and absence without leave, were evaluated throughout our series and graded in order of severity. There appeared to be no obvious relation between severity and degree of record abnormality.

SUMMARY

Electroencephalographic tracings were obtained from 96 of a series of 104 patients with a disorder diagnosed as constitutional psychopathic state in a military setting. Within the special situation from which the patients were obtained, the sample was unselected. The personalities were evaluated first by psychiatric criteria, so that the finding of electroencephalographic abnormality did not influence diagnostic judgment. The records were classified in accordance with the Gibbs criteria with the single exception that records showing certain slow dysrhythmias of paroxysmal character were classified with records of paroxysmal activity rather than with those containing slow sequences. The percentage of abnormal records did not greatly exceed the reported incidence of abnormality in normal control groups studied by different investigators, although we did obtain a definitely higher percentage of records with F-2 and S-2 frequencies than has been obtained for normal controls. We find no relationship between the severity of different manifestations of psychopathy and the incidence of abnormality in records.

FLEXIBLE ELECTRODE-CARRYING HEADGEAR FOR ELECTROENCEPHALOGRAPHIC EXAMINATION

A. R. McINTYRE, M.D.
AND
A. L. DUNN, M.A.
OMAHA

THERE are several advantages to be gained by the employment of a mechanical device for carrying the electrodes used in making contact with the scalp in electroencephalographic examinations. Any method using gauze or other types of bands to hold the electrodes in place is uncertain and unwieldy. The technic which utilizes collodion or similar cementing material to fasten the electrodes is somewhat slow and for best results requires a skilled operator to apply and to remove the electrodes. There is a need for a means of shifting pairs or groups of electrodes rapidly to any part of the skull, as in delineating a tumor. In the interests of obtaining maximum cooperation from the patient, especially with children, the time of examination should be kept to a minimum when possible and the necessary record obtained rapidly.

With these considerations in mind, work was undertaken to develop a mechanical device which would aid in solving these problems. Particular attention was focused on designing an electrode and a means for mounting it which would be sufficiently flexible; several methods were tried and discarded in favor of the system finally decided on.

DETAILS OF CONSTRUCTION

The oval band is constructed of ⅛ inch (32 mm.) fiber, having such dimensions as to allow approximately 2 to 3 inches (5 to 7.5 cm.) clearance all around when placed over a man's head of average size (fig. 1). On this oval band are mounted two fiber straps carrying two electrodes each and so shaped as to maintain 2 to 3 inches clearance around the scalp. The electrodes carried on these straps are intended primarily to make contact with the frontal and parietal areas in a routine examination (fig. 2) but are arranged so flexibly that any portion of the scalp from the occipital to the frontal region can be reached

This work was aided in part by a grant from the Johnson and Johnson Foundation.

From the Department of Physiology and Pharmacology, University of Nebraska College of Medicine.

effectively. Owing to the special construction of the electrode system, several electrodes may be mounted on any of the bands for exploring particular areas of the scalp.

The entire assembly can be clamped to a cot by means of a bracket which embodies a padded neck rest adjustable for height (fig. 3). A hinge (with a locking device) is provided in this bracket, which makes

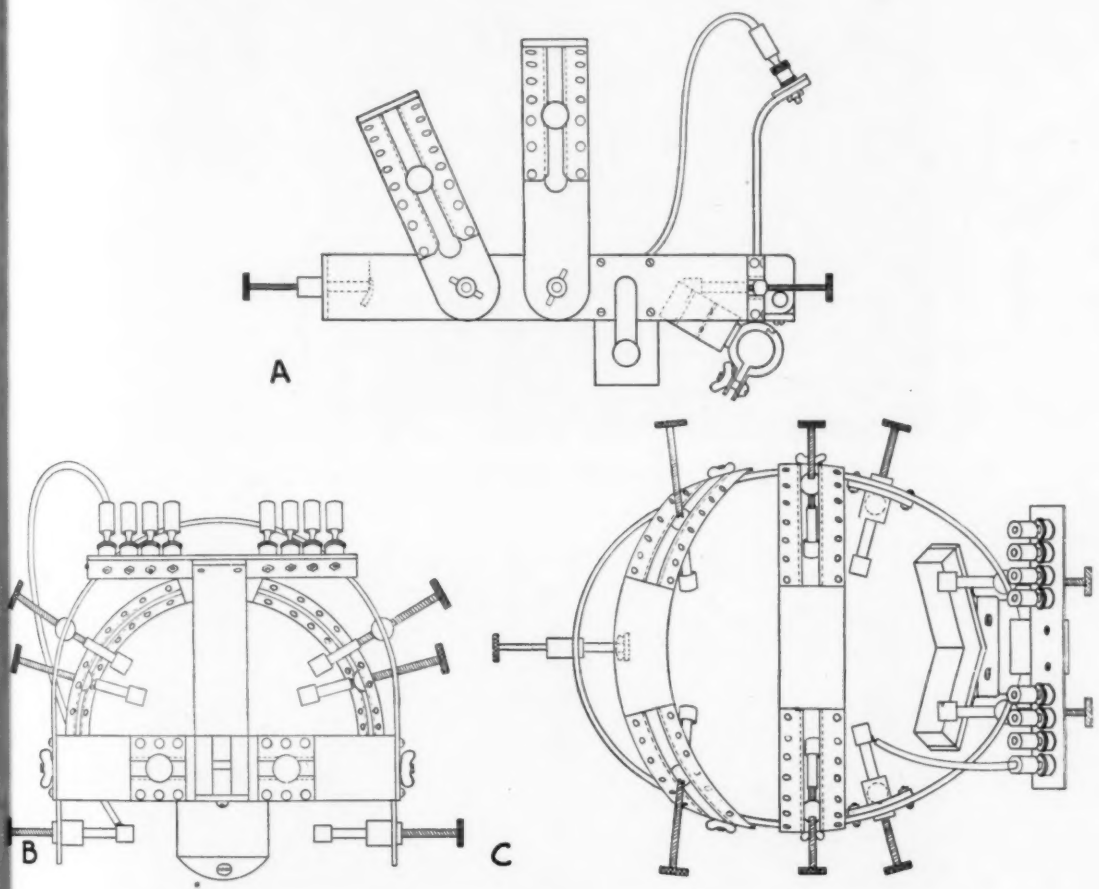


Fig. 1.—Diagrams showing three views of the electrode-carrying headgear.

it possible to swing the headgear over the patient's head quickly and easily. The assembly is held in alinement with the patient's head by means of a padded spring tension nose piece, which bears lightly but firmly on the bridge of the nose and the forehead. Maintenance of the headgear in position is also aided by the mastoid electrodes. The bracket which clamps the headgear to the cot carries all the weight of the device, none of it being allowed to bear on the patient's head.

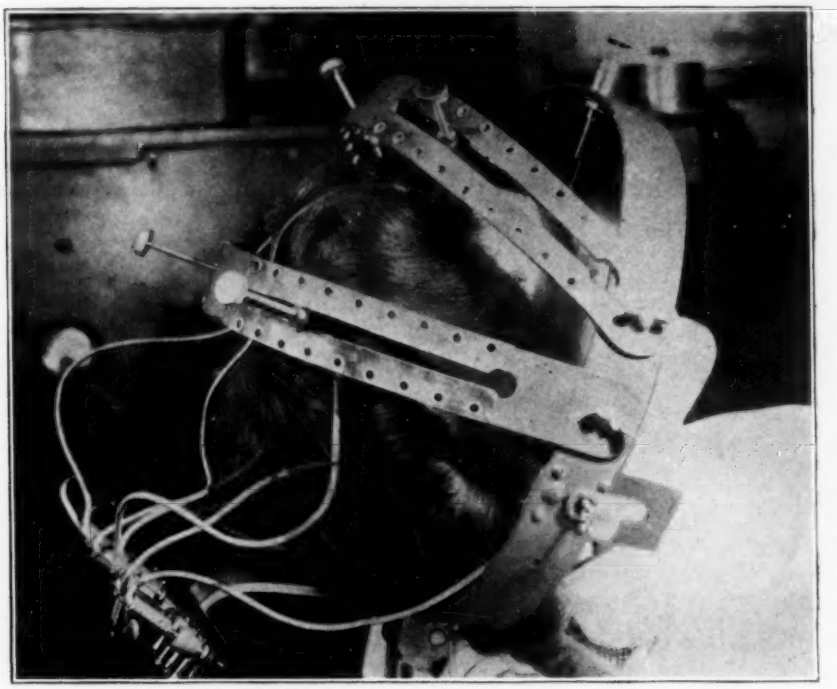


Fig. 2.—Electrode-carrying headgear in place for recording.

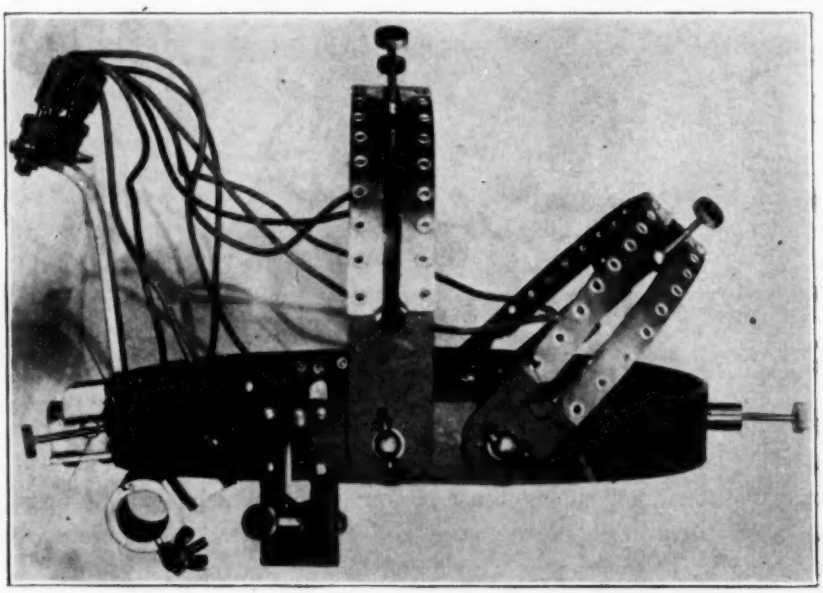


Fig. 3.—General view showing adjustable clamp for cot.

ELECTRODE DETAIL

The frontal, parietal and occipital electrodes are constructed similarly (fig. 4). A contact cup (*A*) is arranged to swivel on the end of the shaft (*C*) and is provided with light tension by a spring (*B*). This

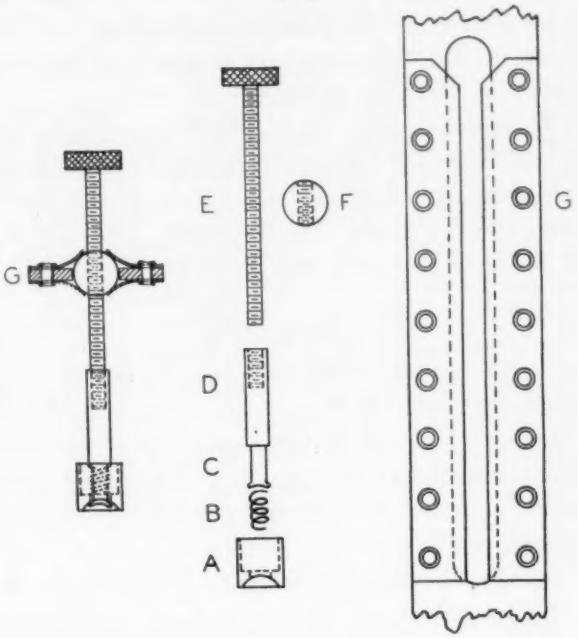


Fig. 4.—Diagrams showing details of electrodes.

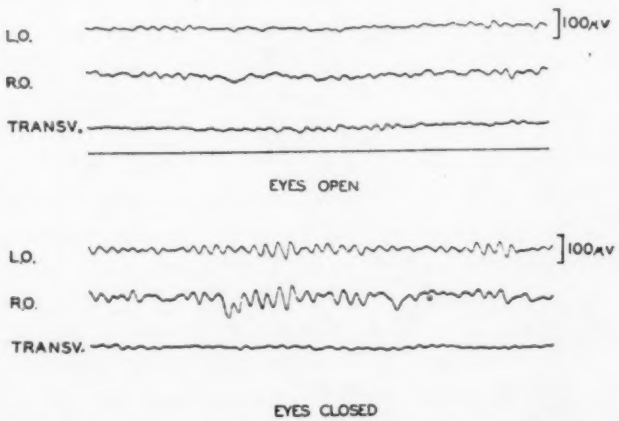


Fig. 5.—Sample record obtained with the headgear.

allows for automatic conformation to the scalp. An insulating link (*D*) of polystyrene or other similar material is interposed, and this entire device is carried on a threaded adjusting rod (*E*), which passes through a

threaded ball (*F*). This ball works in a slide (*G*) built into the adjustable bands of the headgear. Slots equal in width to the diameter of the ball are cut in the bands, and brass-guiding strips are eyeleted to the straps to give a sliding arrangement. An opening is provided at the end of each slide to allow for introduction of additional electrodes.

The mastoid electrodes differ only in having the ball (*F*) contained in a conventional socket, which may be moved in a slot in a fiber piece extending below the oval section.

All metal parts are finished in nickel plate. The connections from the electrodes are brought up to a terminal board, whence they proceed to the electroencephalograph. Electrode jelly is used to facilitate contact between the electrodes and the scalp. A sample of a record obtained with the headgear is shown in figure 5.

SUMMARY

A flexible electrode assembly for use in electroencephalographic examination has been developed.

A rapid means of applying and removing the electrodes is provided.

The special construction of the electrodes allows great flexibility in routine examination or in exploring specific areas of the scalp, as in delineating tumors of the brain.

The time for the examination has been reduced to a minimum for both patient and operator.

* University of Nebraska College of Medicine.

A CLIP-ON ELECTRODE FOR USE IN ELECTROENCEPHALOGRAPHY

DOROTHY L. NIXON
NEW HAVEN, CONN.

IT IS assumed that most electroencephalographic laboratories employ a more or less standard type of electrode, viz., a flattened solder pellet, which is attached to the scalp with collodion.

For several years my associates and I have utilized a convenient clip-on electrode which was adapted from a somewhat similar type of electrode, as described by Darrow[1] in 1940. This clip-on type of electrode eliminates the application of collodion, thereby accelerating the procedure of applying electrodes. It is simply and securely attached to the scalp without discomfort to the patient. This method can be applied only when the patient has a sufficient amount of hair.

Simultaneous recordings made with solder pellet and clip-on electrodes were found to be identical.

CONSTRUCTION AND APPLICATION OF THE CLIP-ON ELECTRODE

A rust-resistant metal is preferred if it is available, but we have found that any semipliable metal can be used. As an item of convenience, we have found that ether cans afford satisfactory results.

Two flat pieces of metal are cut, one approximately 2 by 1 cm. and another approximately 2.5 by 0.5 cm. These strips of metal may be cut either slightly larger or slightly smaller, but the given dimensions will make an average-sized electrode. The wider piece is bent lengthwise, just enough space being allowed to insert the smaller piece, or the electrode "lever" (fig. 1 *A*). After the lever is inserted, the lower corner of the electrode is cut off to permit freedom of the lever when in motion, and the corners of the projecting lever edge are cut off or filed down to facilitate handling (fig. 1 *B*). Next, a hole is punched entirely through the layers of metal, approximately 2 mm. from the top of the electrode and above the clipped under edge. A piece of sturdy wire is then inserted through the perforation and soldered to each side of the electrode to hold it firmly in place. This device is then mounted and soldered to the outer surface of a cup to form the base of the electrode

From the Laboratory of Electroencephalography, Department of Psychiatry and Mental Hygiene, Yale University School of Medicine.

1. Darrow, C. W.: Convenient Electroencephalographic Electrode, Proc. Soc. Exper. Biol. & Med. **45**:301-302 (Oct.) 1940.

(fig. 1 *C*). The cup is merely a no. 3 round head brass paper fastener of which the stem has been removed and the rounded under edge has been filed off to permit thorough cleansing after use. (We utilize this cup type of electrode, applied with collodion, when there is not a sufficient amount of hair to apply the clip-on type of electrode.) One end of the usual electrode wire is then soldered to the outer surface of

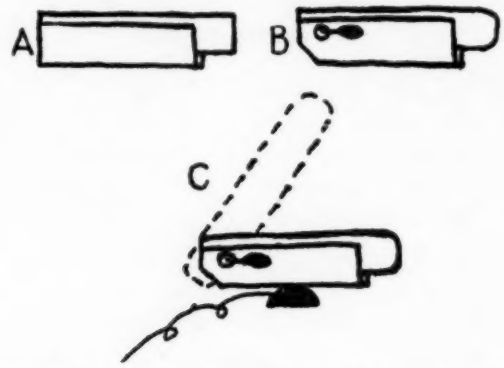


Fig. 1.—Diagrams showing construction of the clip-on electrode.

the cup, and the electrode is ready for use. Photographs of the clip-on electrode as seen from three different angles are shown in figure 2.

To apply the clip-on electrode, the cup is filled with electrode paste. The hair is separated in the usual manner; the scalp is rubbed well with electrode paste, and the electrode is placed on the exposed scalp. With

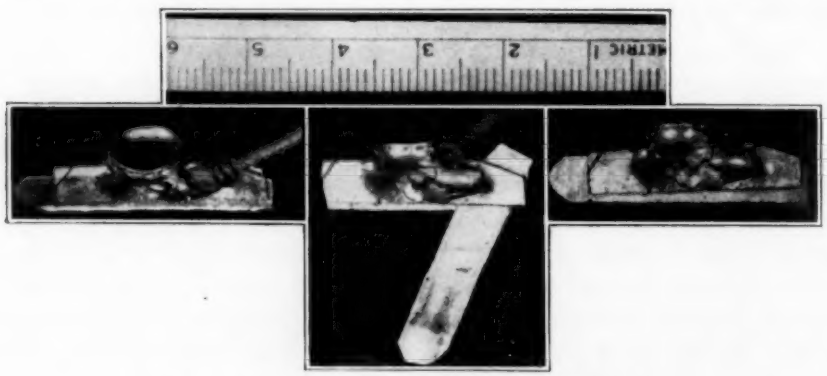


Fig. 2.—Three views of the clip-on electrode.

the lever in an upright position, a few strands of hair are drawn from either side and across the electrode, and the lever is gently pushed to a closed position over the strands of hair.

An electrode of this type will last indefinitely if it is thoroughly cleansed, preferably with acetone, after each application. If the electrode is not properly cleansed, it is likely to deteriorate quickly. A film is

apt to form on the inner surface of the cup, which may cause artefacts, but this film can easily be removed by scraping the cup with a sharp instrument and a clean surface insured.

CONCLUSIONS

The construction of a clip-on electrode is described. This type of electrode has a particular advantage over the more common solder pellet electrode in that it eliminates the usual application of collodion, thereby saving a great deal of time. This electrode can be simply and quickly applied to the scalp without discomfort to the patient. Simultaneous recordings made with solder pellet and clip-on electrodes were found to be identical.

Yale University School of Medicine.

Obituaries

CLEMENT BUCHANAN MASSON, M.D.
1898-1946

Dr. Clement Masson, who became acting chief of neurological surgery in the Neurological Institute of New York on July 1, 1946, died on Sept. 5, 1946 of coronary occlusion at the age of 48. Having served on the house staff of the Neurological Institute from 1925 to 1927, he was the first of the Neurological Institute–trained neurosurgeons to be invited to join the attending staff, and served continuously for nineteen years. His background of neurologic experience and his enjoyment of service under inspired teachers of organic neurology allowed him to carry on the traditional clinical approach to neurosurgical problems, stimulating the younger men on the service with the same spirit with which his predecessors had imbued him.

Dr. Masson was born in Newburgh, N. Y., of Scottish ancestry, in which he took great pride. His academic training was in Washington College, Washington, D. C., from which he received the degree of Bachelor of Science in 1921, after he had received his four years of medical training and the degree of Doctor of Medicine at George Washington University Medical School. He then interned for one and one-half years at St. Elizabeths Hospital, Washington, D. C.; for two years at St. Luke's Hospital, New York, and for two years in the Neurological Institute of New York. He became an assistant surgeon in the Neurological Institute of New York in 1927 and assistant in neurology in the Columbia University College of Physicians and Surgeons in 1928 and progressed through successive grades of promotion in these two institutions, being respectively attending neurologic surgeon and assistant clinical professor of neurologic surgery at his death.

Dr. Masson was not a prolific contributor to the neurosurgical literature, but his report on "Complete Removal of Two Tumors of the Third Ventricle" (*Arch. Surg.* **28:** 527 [March] 1934) is, in a way, a gage of the cautious, constructive and realistic approach he used in attacking the great technical and therapeutic problems of his special field, and of the increasing confidence which it earned him among his colleagues in the Neurological Institute and in the many hospitals surrounding the city in which he consulted. His studies on "The Parasagittal Gliomas" and "The Differential Diagnosis of Parasagittal Gliomas and Parasagittal Meningiomas" (*Bull. Neurol. Inst. New York* **3:** 546 [March] 1934 and **5:** 218 [Aug.] 1936), and his unpublished

studies of the importance and significance of the vestibular tests in the differentiation of lesions in the posterior fossa permitted him to contribute much to the lore and the judgment of the succession of house officers who received practical training under him.

His independent observations in a series of cases concomitant with those of the late Dr. Cornelius Dyke and Dr. Leo Davidoff led to their combined publication of the rather important paper on "Cerebral Hemiatrophy with Homolateral Hypertrophy of the Skull and Sinuses," (*Surg., Gynec. & Obst.* **57:** 588 [Nov.] 1933).

Dr. Masson was a fellow of the American College of Surgeons and was certified by the American Board of Neurological Surgery. He was a member of the St. Andrews Society.

He was attending neurologic surgeon at Grasslands Hospital, Valhalla, N. Y.; Pilgrim State Hospital, and Rockland State Hospital. He was consultant neurologic surgeon at Northern Westchester Hospital, Mount Kisco, N. Y.; Vassar Brothers Hospital, Poughkeepsie, N. Y., and Staten Island Hospital and St. Vincent's Hospital, Staten Island.

To many of us in whose progress Dr. Masson was genuinely interested and to whom, in an impersonal metropolis, he provided a measure of fellowship and an example of a successful career based on a well tempered personality, his untimely passing has been a great shock. By the many to whom his measured opinion, his constant readiness and his seemingly boundless capacity to serve have been a boon, his loss has been keenly felt.

FRITZ CRAMER, M.D.

News and Comment

THE SCIENTIFIC EXHIBIT, ATLANTIC CITY SESSION OF THE AMERICAN MEDICAL ASSOCIATION

At the Atlantic City Session, June 9 to 13, 1947, the American Medical Association will observe its centennial anniversary. For almost half of those hundred years—since 1899—the Scientific Exhibit has been a feature of each annual session and has developed into a short course in graduate medical instruction.

Exhibits at the 1947 Session will cover all phases of medicine. A certain amount of historical material will be included, but emphasis will be placed on the latest developments of medical science. The representative to the Scientific Exhibit from the Section on Nervous and Mental Diseases is Dr. A. B. Baker, University of Minnesota Medical School, Minneapolis.

Applications for space should be submitted as early as possible, since the closing date is Jan. 13, 1947. Application blanks may be obtained either from Dr. Baker or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10.

AMERICAN BOARD OF NEUROLOGICAL SURGERY

The following candidates were recently granted certificates by the American Board of Neurological Surgery:

Oct. 13, 1946: George Ehni, Temple, Texas; Howard H. Karr, Chattanooga, Tenn.

Oct. 14, 1946: John T. B. Carmody, Worcester, Mass.; Joseph F. Dorsey, Boston; J. A. Mufson, Milwaukee; W. W. McKinney, Houston, Texas; Aage Nielsen, Detroit; W. H. Sweet, Boston; Max Taffel, New Haven, Conn.; M. Frank Turney, Brooklyn; Robert D. Whitfield, Albany, N. Y.

Oct. 15, 1946: Charles E. Dowman, Atlanta, Ga.; Antonio Grino, New York; Henry L. Heyl, Hanover, N. H.; Wilfred Risteen, Augusta, Ga.

Dec. 15, 1946: Charles E. Troland, Richmond, Va.

Feb. 1, 1947: Everett F. Hurteau, Memphis, Tenn.; I. Joshua Speigel, Chicago.

NORTH PACIFIC SOCIETY OF NEUROLOGY AND PSYCHIATRY

The North Pacific Society of Neurology and Psychiatry held its annual meeting in Portland, Ore., Sept. 20-21, 1946. The following officers were elected for the coming year: president, Dr. Ralph M. Stolzheise, Seattle; vice president, Dr. Frank Turnbull, Vancouver, British Columbia, Canada, and secretary-treasurer, Dr. Herman A. Dickell, Portland, Ore. The executive committee appointed were: Dr. H. Ryle Lewis, Spokane, Wash.; Dr. Gordon Hutton, Vancouver, B. C., and Dr. Merle Margason, Portland, Ore.

The next meeting of the society will be in Seattle late in March 1947.

Communications may be addressed to Herman A. Dickel, M.D., secretary-treasurer, 707 Medical-Dental Building, Portland 5, Ore.

SCHOOL OF APPLIED PSYCHOANALYSIS

School of Applied Psychoanalysis: Extension Courses of the New York Psychoanalytic Institute.—The academic year, which extends from Sept. 23, 1946 to June 13, 1947, inclusive, is divided into trimesters of (usually) twelve evenings each. The following courses will be given:

A. For Qualified Physicians.—"Relationship of Physicians and Patients in the Light of Psychoanalysis," Dr. Ralph M. Kaufman, in cooperation with Dr. Harry Weinstock and Dr. Sidney Margolin; "Psychoanalysis and Dentistry," Dr. Henry M. Hart; "Sexual Pathology," Dr. Sandor Lorand; "Psychoanalytic Psychopathology," Dr. Nathaniel Ross; "Problems of Child Development," Dr. Margaret S. Mahler; "Indications and Contraindications for Psychoanalytic Psychotherapy," Dr. Samuel Atkin; "Principles of Psychosomatic Medicine," Dr. Lawrence S. Kubie.

B. For Nurses.—"Introduction to Psychoanalytic Psychiatry for Nurses," Parts 1 and 2, Dr. John Frosch.

C. For Social Workers.—"Case Seminar for Psychiatric Social Workers": Part 1 by Dr. I. P. Glauber and Dr. Abram Blau; Part 2 by Dr. Abram Blau and Dr. I. P. Glauber.

D. For Psychologists.—Study Group in "Psychologic Diagnostics," Dr. Lawrence S. Kubie; study group in "Psychoanalytic Psychology," Dr. Heinz Hartmann, Dr. Ernst Kris, Dr. Rudolph Loewenstein and Dr. René Spitz.

E. For Sociologists.—Study groups in "Psychoanalysis and Sociology" and "Psychoanalysis and the Social Sciences," Dr. Robert Waelder (both these courses under consideration).

PENNSYLVANIA PSYCHIATRIC SOCIETY

The eighth annual dinner meeting of the Pennsylvania Psychiatric Society was held at the Barclay, Philadelphia, on Oct. 10, 1946.

Former United States Supreme Court Justice Owen J. Roberts spoke on "What the Layman Can Do About Mental Illness."

The following officers were elected to serve for the year 1946-1947: president, Charles H. Henninger, M.D., Pittsburgh; president elect, LeRoy M. A. Maeder, M.D., Philadelphia, and secretary-treasurer, Philip Q. Roche, M.D., Philadelphia.

Councillors elected were: For two years, Samuel B. Hadden, M.D., Philadelphia; Harold L. Mitchell, M.D., Pittsburgh, and Howard K. Petry, M.D., Harrisburg, Pa. For one year, Bernard J. Alpers, M.D., Philadelphia; Kenneth E. Appel, M.D., Philadelphia; Thomas A. Rutherford, M.D., Waymart, Pa., and Cornelius C. Wholey, M.D., Pittsburgh.

Auditors elected were: For three years, Elmer V. Eyman, M.D., Philadelphia; for two years, Robert J. Phifer, M.D., Woodville, Pa., and for one year, Harry F. Hoffman, M.D., Allentown, Pa.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

DEMONSTRATION OF VISCERAL PAIN BY DETERMINATION OF SKIN POTENTIALS. LESTER M. MORRISON and ERNEST A. SPIEGEL, Ann. Int. Med. **22**:827 (June) 1945.

Morrison and Spiegel report their observations on 72 subjects in an effort to determine whether viscerogalvanic reaction may be an aid in the differential diagnosis of the pain of organic visceral disease and that of nonorganic disorders. The method employed is a variation of the technic described by Spiegel and Wohl. In this method a known variable potential is opposed to the unknown skin potential.

The authors conclude that the study of skin potentials is an objective method useful in the evaluation of visceral pain. In 74 per cent of the 31 patients with pain accompanying proved organic visceral disease the skin potentials in the corresponding dermatomes were increased over those in the rest of the body by 10 or more millivolts. Of 27 patients with pain of psychogenic origin or pain associated with healed organic disease, 2 showed increases in potential of 8 and 9 millivolts, respectively, while the other 25 had no increase of potentials.

An increase in skin potentials of 10 millivolts or over in the dermatomes corresponding to an organ causing pain supports the assumption of organic disease. Absence of increased potentials does not exclude organic disease. After apparent clinical healing of organic visceral disease, increased potentials may still persist, indicating latent pathologic changes.

GUTTMAN, Philadelphia.

NERVE REGENERATION IN THE RAT FOLLOWING TUBULAR SPLICING OF SEVERED NERVES. P. WEISS, Arch. Surg. **46**:525 (April) 1943.

Weiss describes a new method of union of severed peripheral nerves which in animal experiments (23 rats) has proved superior to the conventional nerve suture and may be adaptable to human surgery. The method, which should not be confused with the old "tubulization" technic, consists in splicing the two ends of a severed nerve by inserting them into a closely fitting sleeve of a live artery. The use of the arterial sheath eliminates the need of foreign suture material, which may impair nerve regeneration. The tensile strength obtained by the arterial method of nerve splicing is greater than that of the sutureless union of nerves by blood plasma. The utilization of an artery in nerve splicing is particularly suited for nerves too small for suture. The arterial link permits leaving a slight gap between the nerve ends, which seems to create favorable conditions for nerve regeneration. Longitudinal stresses are transmitted through the tissue matrix filling the gap between the two nerve ends and produce parallel orientation of the regenerating nerve fibers. Thus, an orderly regeneration of nerve fibers is assured, and a good functional result may be expected. Histologic study showed that the nerve fibers regenerate in parallel rows, without irregular branching or formation of neuroma or scar tissue. The region of the gap is discernible only by the absence of perineurium. A count of nerve fibers revealed close correspondence between the number of fibers in the proximal stump and the number of regenerated fibers in the gap, but there was a drop in the fiber count in the distal stump. Only a few physiologic observations were made on the functional recovery of spliced nerves. Return of muscle power, measured by isometric recording

after supermaximal stimulation of the spliced nerve, showed return to normal contraction in some instances as early as ten weeks; in other cases the muscular contraction remained deficient, even though there was histologic evidence of good regeneration. Coordination remained poor, in spite of good motor and sensory recovery. This was presumably due to random redistribution of regenerated fibers. Some arterial nerve splicings failed because of improper width of the artery or trauma to the arterial wall. In these cases, fibrosis and irregular regeneration of nerve fibers occurred, or nerve fibers escaped through a defect in the arterial wall.

LIST, Ann Arbor, Mich.

CONVULSIVE FACTOR IN COMMERCIAL PENICILLIN. A. EARL WALKER and HERBERT C. JOHNSON, Arch. Surg. **50**:69 (Feb.) 1945.

Walker and Johnson studied the effect of commercial penicillin applied topically to the cerebral cortex of the cat, dog, monkey and man. In the cat, as little as 1,000 to 2,000 Oxford units of penicillin may cause convulsive manifestations; in man the convulsive threshold is approximately 10,000 or 20,000 units. The convulsive and antibiotic factors of penicillin appear to be closely related, for they are about equally affected by aging, boiling and acidifying the penicillin solution and by dissolving the penicillin in alcohol.

LIST, Ann Arbor, Mich.

INHIBITION OF BRAIN RESPIRATION BY PICROTOXIN. J. R. KLEIN, J. Biol. Chem. **151**:651, 1943.

Although the stimulatory effect of picrotoxin on the central nervous system is well known, there is little information concerning the effect of the drug on the metabolism of brain. The respiration of a cat brain preparation and the oxidation of glutamate, succinate, fumarate and pyruvate by the preparation in vitro were inhibited by picrotoxin. The effect of the drug on glutamate and succinate was probably due to an inhibition of the oxidation of fumarate or pyruvate rather than its action on the first stages in the oxidation of the former substances. The effect of picrotoxin on the oxidation of pyruvate may have been due to inhibition of fumarate catalysis, since fumarate decreased the extent of inhibition.

PAGE, Cleveland.

A PARALLELISM BETWEEN THE QUANTITATIVE INCIDENCE OF CARBONIC ANHYDRASE AND FUNCTIONAL LEVELS OF THE CENTRAL NERVOUS SYSTEM. W. ASHBY, J. Biol. Chem. **152**:235, 1944.

Since it has been shown that the greater amount of carbonic anhydrase per gram in the functionally dominant cerebral area than in the cord is not dependent on any anatomic distribution of gray and white matter, the possibility is suggested that the relation may be due to differences in the amount of enzyme contained in the neurons entering into the composition of the respective areas. This might be true regardless of whether the cell processes or the cell body of the neuron establishes the preponderance of the enzyme. On this basis, it is probable that the carbonic anhydrase content may bear a relation to the factors which cause the functional dominance of the cerebrum over the cord. As a second possibility, the carbonic anhydrase may not be distributed in the neurons but may exist in some accessory cells, which may be more numerous in the cerebrum than in the cord. The content of carbonic anhydrase in the cerebral tissue and in the cord tissue has now been compared. The content of the cerebral tissue was approximately twice that of the cord. Seven species of animals were studied. By separate determinations of the enzyme content of the white matter of specimens of the human cerebrum, it was shown that the greater amount of enzyme in the cerebrum is not due to the larger proportion of gray matter present.

PAGE, Cleveland.

CHOREIFORM MOVEMENTS IN A DOG SUFFERING FROM CORTICO-STRIATAL DISEASE. HSIANG-TUNG CHANG, J. Neurophysiol. **8**:89 (March) 1945.

Chang described a male dog with nodding movements of the head and rapid, involuntary twitchings of the left hindleg. The animal demonstrated a postural disturbance in that he could not curl his trunk, and he also could not properly scratch himself. These difficulties were ascribed to rigidity of the muscles. In addition, there was some motor deficit. During a three month period of observation the disturbances were stationary. With the animal under anesthesia, it was noted that excitability of the right motor cortex was decreased. Histopathologic examination of the brain revealed congestion of the cerebral blood vessels, some endothelial proliferation in the walls of the blood vessels, infiltration of the meninges and evidence of encephalitis. The encephalitic lesions consisted of perivascular lymphocytic infiltration and gliosis. The lesions occurred in the left putamen and the adjacent insular cortex and in the right hemisphere in the region of the posterior sigmoid gyrus. In the last area the outer layers of the cortex were not involved, and the giant pyramidal cells were spared. Chang concludes that for the production of choreiform movements preservation of part of the motor cortex is necessary but that both motor cortex and putamen must be damaged.

FORSTER, Philadelphia.

ELECTROENCEPHALOGRAM OF DIFFERENT CORTICAL REGIONS OF NORMAL AND ANESTHETIZED CATS. SAM. L. CLARK and JAMES W. WARD, J. Neurophysiol. **8**:99 (March) 1945.

Clark and Ward, employing concentric, implanted leads with the stigmatic portion in contact with the brain, studied the electrical activity of the cat cortex and obtained specific patterns from the frontal and occipital regions and from the vertex. Records from the temporal region and from the pyramids showed less characteristic differences. The onset of sleep was accompanied with the appearance of trains of waves of 5 to 7 cycles per second from the occipital leads. When sleep deepened, the frontal region presented 12 to 14 cycle per second spindles, and random slow activity appeared in all leads. Records obtained during sleep induced with pentobarbital resembled those obtained during normal sleep except that the stages followed each other more rapidly in the former. Activation patterns could be produced by stimuli in normal or in light pentobarbital sleep, but with the animal under deep pentobarbital anesthesia no visible changes occurred in the electroencephalogram during operative procedures. Clark and Ward demonstrated that temporary habituation to a standard stimulus in the normal resting animal produces in the electroencephalogram progressively greater shortening of the period of activation. Alteration of the type of stimulus immediately restores the activation response.

FORSTER, Philadelphia.

PROJECTION OF THE RETINA ON THE SUPERIOR COLLICULUS OF CATS. JULIA T. APTER, J. Neurophysiol. **8**:123 (March) 1945.

Apter studied the electric action potentials obtained from the surface of the superior colliculus of the cat. The potentials were evoked by stimulating spots of known position on the retina, and the stimuli used were short flashes of light. She found a systematic projection of the nasal field, or temporal half of the retina, of the left eye on the left superior colliculus and of the temporal field, or nasal half of the retina, of the right eye on the right superior colliculus. The nasal half of the left area centralis projected only on the right superior colliculus, and the temporal half of the left area centralis projected only on the left superior colliculus. The upper field, or lower half of the retina, was projected on the superior colliculus medial to the lower field, or upper half of the retina. Points along the vertical meridian were projected at the anterior end of the superior colliculus. Points 110 degrees temporal to the vertical meridian of the visual field

of the left eye were at the posterior end of the right superior colliculus, and points 90 degrees nasal to the vertical meridian were at the posterior end of the left superior colliculus.

. FORSTER, Philadelphia.

Neuropathology

FATAL POISONING FROM POTASSIUM THIOCYANATE USED IN TREATMENT OF HYPERTENSION. ANTONIO DEL SOLAR, GASTON DUSSAILLANT, MOISES BRODSKY and GUILLERMO RODRIGUEZ, Arch. Int. Med. **75**:241 (April) 1945.

The authors report a case of a 53 year old white man with hypertension who was treated with potassium thiocyanate. During the course of treatment he showed mental dulness and increased dysarthria. This was followed by zoopsia and slightly clonic contractures of the upper extremities. Thiocyanate levels in the blood reached 29 mg. per hundred cubic centimeters, and the urinary concentration of the drug was 33 mg. per hundred cubic centimeters. It was then discovered that for about eight or ten days the patient had been taking as much as 1.34 Gm. of potassium thiocyanate a day because he had broken the tip of the dropper. Various supportive measures were attempted after the patient went into coma, but in about two weeks he died.

Necropsy revealed no recent lesions which could account for his death. There were two old areas of encephalomalacia. It is possible that the thiocyanate intoxication came on more readily because of old cerebral damage. A prominent observation in the postmortem examination was an area of acute nephrotic necrosis, which had apparently been asymptomatic during life.

This is the seventh reported instance of death due to therapeutic use of potassium thiocyanate for hypertension.

GUTTMAN, Philadelphia.

PRIMARY DEGENERATION OF THE CORPUS CALLOSUM (MARCHIAFAVA-BIGNAMI'S DISEASE). H. HOUSTON MERRITT and AVERY D. WEISMAN, J. Neuropath. & Exper. Neurol. **4**:155 (April) 1945.

Merritt and Weisman report 2 cases of degeneration of the corpus callosum. The first case was that of a man, aged 50, who was addicted to alcohol and was in a state of poor nutrition. There were associated dementia, transitory hemiparesis, aphasia and convulsions. He had an affective psychosis with a severe obsessive-compulsive component.

Sections of the brain revealed complete cystic degeneration of the middle portion of the corpus callosum. The genu was the most severely affected, although the necrosis extended back to the splenium, where the degenerated tissue consisted of two symmetric areas of reddish softening. The cystic degeneration in the rostral portion of the corpus callosum indicated an older process, while the soft, necrotic character of the bilateral lesions in the posterior part of the body and the splenium suggested a more recent development.

Microscopic observations showed almost complete loss of myelin in the middle lamina of the corpus callosum. At the periphery of the lesion the myelin sheaths had undergone a less degree of damage; they stained poorly and were irregularly swollen and attenuated. The axis-cylinders were relatively intact, even in regions where the demyelination was most advanced. Where cyst formation had occurred, however, all tissue elements were destroyed. Proliferation and hypertrophy of capillary endothelial cells were pronounced, and numerous fat-filled histiocytes infiltrated the affected zone. Gliosis was not well developed.

The second case was that of a man, aged 56, who entered the hospital in a state of stupor. He had sustained a head injury and was in shock. Unfortunately, a complete history could not be obtained, but the patient was blind and deaf and had been living alone. The day prior to admission he had been acting peculiarly, and neighbors thought he was ill. Neurologic examination revealed that the patient was in coma. The arms were flaccid, while both legs were extremely spastic. Tendon reflexes were exaggerated, those on the right side being some-

what more active than those on the left. Plantar responses were flexor. The patient failed to regain consciousness and died.

Examination of the brain disclosed extensive degeneration of the middle zone of the corpus callosum. A thin dorsal and ventral rim of intact tissue remained on either side of the necrotic area. The disease process extended from the genu and the anterior commissure caudally to the splenium.

There were large, symmetric areas of necrosis in the subcortical white matter of the frontal, parietal, temporal and occipital lobes. Each lesion was confluent at some point with the degenerated portion of the corpus callosum. In the temporal lobe, the optic radiations were affected. There was bilateral softening of the middle cerebellar peduncles.

The histologic changes in the corpus callosum in this case were similar to those described in the first case. In the subcortical white matter the affected areas were sharply delineated from the surrounding tissue by many astrocytes. Within the rim of gliosis the myelin sheaths had completely disappeared; only scanty, pyknotic oligodendrocytes, proliferating capillaries and hypertrophic endothelial cells remained. Fat-filled phagocytes were rare. No evidence of inflammation was observed.

In the second case a history of alcoholism could not be verified. The association of blindness and deafness in Marchiafava-Bignami disease has not previously been stressed, and it is of interest that they occurred in connection with extensive damage to the temporal and occipital lobes. The well developed gliosis about the subcortical lesions was an unusual histologic feature.

Merritt and Weisman state that the clinical picture cannot be explained by the callosal lesion but requires postulation of a more diffuse cerebral disorder. Marchiafava-Bignami disease is considered a form of chronic alcoholic encephalopathy, for which an inadequate diet and prolonged alcoholism are necessary antecedents.

GUTTMAN, Philadelphia.

A STUDY OF THE MECHANISM OF VELOPHARYNGEAL CLOSURE. ROBERT HARRINGTON, J. Speech Disorders **9**:325, 1944.

Detailed dissections of the soft palate and pharynx of 10 cadavers were undertaken. The purpose was to investigate the palatal origin of the pterygopharyngeus muscle. The palatopharyngeus and salpingopharyngeus muscles were also studied. In 8 of 10 cases a palatal origin of the pterygopharyngeus muscle was found to exist. In the majority of cases this bundle consisted of a small strand of fibers which originated near the insertion of the levator palati muscle in the palatal aponeurosis, but in all cases a hamular origin of the muscle was also found. The hamular origin was the better developed and was just inferior to the smaller (palatal) origin. In 8 of 10 cases there were muscle connections between the palatopharyngeus and the pterygopharyngeus muscle.

The results of the study suggest the following conclusions: 1. In addition to its hamular division, the pterygopharyngeus receives fibers which originate in the soft palate. 2. The palatal fibers of the pterygopharyngeus may contribute to mesial movement of the pharyngeal walls during velopharyngeal closure. 3. Muscular connections between the palatopharyngeus and the pterygopharyngeus muscle normally exist. 4. Because of these connections, the approximation of the palatopharyngeus muscles during velopharyngeal closure may contribute to the mesial movement of the lateral pharyngeal walls. 5. In addition to the insertions of the palatopharyngeus muscle into the lateral pharyngeal wall, the salpingopharyngeus muscle may occasionally send fibers to the soft palate. 6. The salpingopharyngeus muscle may contribute to velopharyngeal closure by creating an inbulging of the lateral pharyngeal walls. This muscle may also contribute slightly to the elevation of the soft palate.

Four subjects with cleft palate and 1 subject who had a carcinoma of the left maxillary sinus with radical resection were studied for movement of the velum by roentgenographic and other methods.

The general conclusions from both the anatomic and the physiologic studies are as follows: 1. Palatal fibers of the superior constrictor muscle exist and probably account for a part of the anterior and mesial movement of the pharyngeal walls. 2. Muscular connections between the palatopharyngeus and the pterygopharyngeus exist and may account for some of the mesial movement of the pharyngeal walls. 3. Anatomic relationships of the salpingopharyngeus suggest that this muscle probably acts to raise the velum and to move the lateral walls of the pharynx in a mesial direction. 4. Considerable mesial movements of the lateral pharyngeal walls exist. 5. Mesial movement occurs over a considerable vertical extent. Movement may be greater at a lower level than at the higher position. 6. The amount of mesial movement is directly related to the extent of velar elevation. 7. The greatest extent of mesial movement appears to occur in the area overlying the salpingopharyngeus muscle. 8. Although there are significant differences between certain vowel sounds in regard to velar and mesial pharyngeal movements, these differences are not significant for the anterior movement of the posterior pharyngeal wall. 9. The velopharyngeal mechanism does not function as a simple sphincter.

PALMER, Wichita, Kan.

OLIVOPONTOCEREBELLAR ATROPHY. OSCAR LUQUE and RAUL PUCHETA MORCILLO, Rev. argent. de neurol. y psiquiat. **10**:17 (March) 1945.

The authors report the case of a man aged 57 in whom weakness developed in all four limbs three years before admission; progressive impairment of speech was also observed. For eighteen months prior to admission the patient was bedridden because of weakness. For a time after the onset the lower limbs became tremulous on his attempting to walk. For three months he complained of blurring of vision even during very short periods of fixation. There was a history of mild, inconstant dysphagia.

Objective examination showed inability to sit up properly; the patient laughed readily; there were marked hypomimia and weakness in both lower branches of the facial nerve; the tongue was flabby and could not be protruded normally; use of the tongue in speech was definitely impaired; the masseter reflexes were exaggerated; no dysphagia was apparent; there was weakness of all the limbs; dysdiadiadokokinesis was present bilaterally, especially on the left; weakness in the upper extremities was more pronounced on the left; there were dysmetria and dyssynergia in the upper limbs, especially on the left; the tendon reflexes of the arms were hyperactive; the knee jerks were exaggerated, especially on the left; there was a bilateral ankle clonus, which was stronger on the left; the abdominal reflexes were diminished on the left; the Babinski sign was elicited on the left, and there was poor plantar flexion on the right; Oppenheim and Gordon signs were present on the right; dysmetria and asynergia were pronounced in both lower limbs. Examination of the spinal fluid revealed nothing abnormal. The patient died of pneumonia, five years after admission.

Postmortem examination showed evident atrophy of the middle cerebellar peduncles and atrophy of the cerebellum, especially the superior surface. Both the vermis and the hemispheres were involved. Conspicuous depressions, due to diminution of white substance, were seen in both quadrilateral lobes. Histologic examination showed demyelination of almost all the white substance of the cerebellum. The intraolivary plexus from which fibers of the superior cerebellar peduncles arise was spared. Fibrillary gliosis was observed in the demyelinated areas. The dentate nuclei were entirely spared, but some of the cells were abnormally pigmented. The myelin fibers deep in the white substance were extensively broken up. The association fibers were not so seriously involved. The Purkinje cells had disappeared. The granular cells were also much diminished in number, apparently in proportion to the extent of involvement of the Purkinje cells. The basket cells remained but had become flattened transversely and enlarged vertically as the Purkinje cells disappeared. Structures in the granular layer, previously described as dilatations of the axis-cylinders of the Purkinje

cells, are considered by the authors to be their cell bodies pulled out of place. The reasons given for this hypothesis are that intact Purkinje cells are not encountered in the presence of these dilatations; careful histologic studies showed Nissl substance, chromatin and structures resembling nuclei and nucleoli in these structures. There were pallor of the pyramidal tracts in the bulb and cord and disappearance of cells of the olives and of the olivocerebellar fibers. The restiform bodies were about one-fifth the normal size. The whole of the middle cerebellar peduncle had disappeared, with almost all the cells of the pontile nuclei gone and replaced by intense gliosis. The authors believe that the pseudobulbar features were due to impingement of the intense gliosis on the pyramidal tracts in the pons.

SAVITSKY, New York.

Meninges and Blood Vessels

HEPATORENAL FAILURE IN THE WATERHOUSE-FRIDERICHSEN SYNDROME. BRUNO A. MARANGONI and VINCENT C. D'AGATI, Am. J. M. Sc. **207**:385 (March) 1944.

Marangoni and D'Agati report 2 new cases of the Waterhouse-Friderichsen syndrome which they encountered in the treatment of 134 cases of meningococcic infection at a station hospital.

The first case was that of a man aged 20 who was admitted to the hospital on Jan. 24, 1943 with a diagnosis of infection of the upper respiratory tract. On the eighth day the patient became desperately ill; he was pallid, apprehensive, restless and in severe shock. Numerous petechiae and purpuric lesions were distributed over the entire body. Facial edema was observed, particularly about the eyes. A blood count revealed 47,250 white cells, with 94 per cent polymorphonuclear leukocytes.

A diagnosis of an overwhelming meningococcemia with adrenal hemorrhages (Waterhouse-Friderichsen syndrome) was made. The patient was given a 5 per cent solution of sodium sulfadiazine intravenously (5.5 Gm. in 111 cc. of sterile distilled water). A total of 80,000 units of meningococcus antitoxin was given intravenously within the first eighteen hours of therapy. Colonies of Neisseria intracellularis type II-IIa were grown from the blood culture. The patient died on the eleventh day in the hospital, eighty hours after the onset of the Waterhouse-Friderichsen syndrome.

The most striking observation at autopsy was the appearance of the adrenal glands, which together weighed 15 Gm.. They showed hemorrhagic areas, particularly in the left gland. Microscopic examination revealed histologic changes in the adrenals, liver and kidney. The hemorrhages in the adrenals were of varying sizes and involved both the cortical and the medullary area. In the liver, there were engorgement of the central vein and sinusoids and marked dissociation of the hepatic cords; many of the cells showed necrobiosis, and many others were heavily laden with bile pigment. The kidneys showed increased cellularity and avascularity of the glomerular tufts; focal areas of polymorphonuclear infiltration and interstitial edema were observed.

The second case was that of an obese white man aged 20, who was seriously ill but rational and oriented. There was facial edema with puffiness about the eyes. The body was covered with numerous petechial and purpuric areas. The blood pressure was 60 systolic and 40 diastolic. A blood cell count revealed 66,950 white cells, of which 96 per cent were polymorphonuclear leukocytes. The blood culture was positive for Neisseria intracellularis type I. A diagnosis of fulminating meningococcemia with adrenal hemorrhages (Waterhouse-Friderichsen syndrome) was made. The patient was given 5.5 Gm. of sodium sulfadiazine intravenously in a 5 per cent solution of sterile distilled water. Within the first twelve hours after admission he received a total of 80,000 units of meningococcus antitoxin intravenously. The course was progressively downhill, and the patient died eighty-eight hours after admission to the hospital. The

significant observations at autopsy were moderate congestion of the liver and kidneys. The corticomedullary demarcations of the kidneys were indistinct. The brain revealed marked engorgement of its superficial vessels. The adrenals were hemorrhagic and on microscopic section numerous small hemorrhages were noted involving both the medulla and the cortex. The architecture of the hepatic lobules showed pronounced destructive changes in the central and mid zones. The hepatic cords in these zones were completely destroyed. The authors postulate that their cases represent two clinical stages in the Waterhouse-Friderichsen syndrome. The first, or fulminating, stage is generally recognized and consists of severe shock with circulatory collapse. Survival of this stage ushers in the hitherto undescribed second, or hepatorenal, stage, which is characterized clinically by marked oliguria with azotemia and pathologically by severe toxic hepatitis associated with glomerular and degenerative tubular changes. The life expectancy of the patient is inversely proportional to the degree of adrenal tissue destroyed by hemorrhage.

MICHAELS, A.U.S.

LYMPHOCYTOSIS IN THE CEREBROSPINAL FLUID. IRVING L. APPLEBAUM, JOEL SHRAGER and WILLIAM PAFF, Ann. Int. Med. **23**:170 (Aug.) 1945.

Applebaum, Shrager and Paff report their observations on 72 patients from the Canal Zone who had lymphocytosis of the cerebrospinal fluid, due to a variety of etiologic agents.

A résumé of the conditions producing the lymphocytosis and the statistical data for this series is given in the following tabulation.

Diagnosis	No. of Patients	Percentage
Meningoencephalitis following mumps	30	41.6
Acute lymphocytic meningitis, benign type (cause undetermined)	17	23.6
Syphilis of central nervous system	7	9.7
Tuberculous meningitis	4	5.6
Chemical meningitis (intrathecal injection of serum, etc.)	3	4.2
Acute encephalitis, cause undetermined	2	2.8
Tetanus	2	2.8
Trauma of brain	1	1.4
Abscess of brain	1	1.4
Cysticercosis of central nervous system	1	1.4
Rabies	1	1.4
Lymphocytic meningitis associated with malaria	1	1.4
Guillain-Barré syndrome	1	1.4
Infectious mononucleosis	1	1.4

The clinical patterns of mumps meningoencephalitis and acute benign lymphocytic meningitis are discussed, and the early subsidence of the clinical syndrome with a relative lag in clearing of the pleocytosis was prominent in the cases of both types.

The following clinical classification was submitted as an aid in the differential diagnosis of lymphocytosis in the cerebrospinal fluid:

Acute lymphocytic meningitis (benign)

Acute lymphocytic choriomeningitis
Lymphocytic meningitis due to allied viruses
Aseptic meningitis, cause undetermined (Wallgren).

Other diseases of virus origin

Mumps; acute encephalitis (varieties); poliomyelitis; rabies; herpes (zoster and simplex); common contagions; postvaccination; lymphogranuloma venereum; infectious mononucleosis; Guillain-Barré syndrome

Specific bacterial infections
Tuberculosis; syphilis; tetanus

Fungous and parasitical infections (uncommon)
Torula infection; cysticercosis

Intraspinal infections introduced by chemical substances
Serum; procaine solution; iodized poppyseed oil 40 per cent.

Meningitis sympathica (irritative)
Sequela to trauma of brain, aural infection, subdural abscess, epidural abscess

GUTTMAN, Philadelphia.

PNEUMOCOCCAL MENINGITIS: RECOVERY WITH SULFAMETHAZINE [SULFAMEZATHINE]. R. PAKENHAM-WALSH, Lancet **1**:649 (May 22) 1943.

The author reports the case of a woman aged 68 with pneumococcic meningitis, as proved by smear and culture of the spinal fluid. She received 2 Gm. of sulfamezathine every four hours for five doses, the administration starting the second day of the clinical disease. The third day the dose was changed to 1 Gm. every six hours; this dosage was continued for five days, when she showed signs of cyanosis and use of the drug was stopped. The signs and symptoms subsided a few days later and she was able to walk unaided about the room in a month, but the pleocytosis persisted. She was given 1.5 Gm. of sulfamezathine three times a day for a week, but the pleocytosis persisted and was still present three months after the onset of the illness.

McCARTER, Philadelphia.

Diseases of the Brain

TICK-BORNE ENCEPHALITIS. ANATOL A. SMORODINTSEV, Am. Rev. Soviet Med. **1**:400 (June) 1944.

Smorodintsev reviews some of the studies on spring-summer, or tick-borne, encephalitis. The incubation period is eight to eighteen days. The onset is associated with elevation of temperature, headache, pains in the neck, vertigo and vomiting. Meningeal and focal neurologic signs, followed by paresis and paralysis of the limbs, back and neck, predominate. An ascending type of paralysis with subsequent bulbar involvement develops. The average duration of the acute phase is five to six days, but the acute stage may run its course in two to ten days. The mortality rate ranges from 20 to 30 per cent. Death usually occurs between the third and the eighth day of the disease. Many patients are physically disabled by paralysis and atrophy of the cervical muscles and shoulder girdle. The patients who recover do not display Parkinson's syndrome, which occurs after von Economo's lethargic encephalitis. Spring-summer encephalitis in the European part of the Soviet Union is marked by a milder course, less invalidism and chronicity, with a mortality rate of only 10 per cent.

The histopathology of spring-summer encephalitis is characterized by intense inflammatory and degenerative changes of the nervous system. The pia mater of both the brain and the spinal cord is always involved. An acute serous exudate appears on the meninges; the brain is softened and congested, and numerous hemorrhages appear in the brain stem, the medulla and the horns of the spinal cord. The most extensive lesions occur in the gray matter of the cord and medulla, fewer in the gray matter of the base of the brain and only slight changes in the cortex. The changes consist in acute perivascular infiltration involving the brain stem and meninges and diffuse or focal infiltration of the gray matter. The disease may be classified as acute nonsuppurative meningoencephalopoliomyelitis.

The causative agent is a virus which passes through the finest Berkefeld and Chamberland filters. Monkeys, goats, sheep and white mice and other rodents

are susceptible to the virus. Mice infected with the spring-summer encephalitis virus react like those infected with strains of the St. Louis and the Japanese encephalitis virus. The virus belongs to type B of seasonal encephalitis and cannot be neutralized by the serums of patients recovered from von Economo's lethargic encephalitis. It also differs strikingly from the virus of the St. Louis type in its antigenic and immunogenic properties, since they do not give cross neutralization or immunity. There are antigenic factors common to both the spring-summer and the Japanese encephalitis virus. According to recent observations by Casals, the virus of spring-summer encephalitis bears a close relation to the virus of louping ill through reactions to complement fixation, neutralization and intraperitoneal cross resistance tests, while intracerebral cross resistance tests give negative results. Neither the virus of Russian encephalitis nor the virus of louping ill appears to be related to the viruses of the Japanese, St. Louis and West Nile types of encephalitis.

The virus of spring-summer encephalitis propagates in vitro in cultures of minced chick embryo tissue or when inoculated in developing eggs. The amount of the virus cultured in the egg is distinctly less than that produced in the brain of infected mice.

The systematic increase of specific antibodies in the blood of convalescent patients confirms the role of the virus as the specific causative agent of spring-summer encephalitis. The blood of convalescent persons contains specific antibodies, which are present many years after the initial illness.

The virus of tick-borne encephalitis is indigenous to the forest regions of the Far East, Siberia and the European part of the Soviet Union, the Urals, Karelia, Western Ukraine and White Russia. The disease is distinctly seasonal, beginning at the end of April, assuming epidemic proportions in May and reaching an incidence of 80 per cent between the middle of May and June. Before May and after August only sporadic cases occur. Moderate atmospheric temperature and relatively high humidity favor the development of the disease. The clinical and epidemiologic characteristics of tick-borne encephalitis distinguish it from the Japanese and the St. Louis type, which are most prevalent during the dry, hot summer months of August and September. In Japan and the United States the disease occurs not only in agricultural districts but also in dry, hilly, urban areas, favors no single occupational group and primarily affects persons over 40 years of age. The epidemiologic evidence suggests that the propagation of encephalitis among human beings should be attributed not to contact transmission of the infection but to vectors, such as the blood-sucking arthropods inhabiting the forests, the wood ticks.

The mortality rate of spring-summer encephalitis does not exceed 30 per cent, whereas the mortality rate of summer encephalitis B reaches 60 to 70 per cent and that of the St. Louis form averages 20 per cent. A considerable number of convalescent patients retain residual organic lesions, which is rare with the B and St. Louis forms.

Data are presented which indicate that transmission of the disease is through ticks (Ixodes persulcatus). The transmission of the virus in the encephalitis area may be traced from spontaneously infected larvae and nymphs to rodents or birds, which have a latent or clinical form of encephalitis. These rodents, in turn, transmit the virus to healthy larvae and nymphs, thus completing the cycle.

Prophylactic measures aimed primarily at liquidating ticks and rodents are outlined. Immunization with vaccine prepared from the brains of affected animals and inactivated with solution of formaldehyde is one of the most reliable methods. Evidence is presented which shows the value of use of the formaldehyde-inactivated vaccine as a prophylactic measure. Patients with spring-summer encephalitis were treated with repeated administration of convalescent serum and showed definite improvement.

GUTTMAN, Philadelphia.

BRAIN ABSCESS ASSOCIATED WITH CONGENITAL HEART DISEASE. STANLEY L. ROBBINS, Arch. Int. Med. **75**:279 (May) 1945.

Robbins reports 3 cases of brain abscess associated with septal defects of the heart. They were selected from the necropsy material, comprising 7,080 cases, at the Mallory Institute of Pathology of the Boston City Hospital during the years 1936 to 1943. This material included 53 cases of congenital heart disease of all types.

The first case reported was that of a 10 year old girl who had a history of listlessness and extreme lethargy for seven days. There was also a persistent cough for three or four days, followed by intractable vomiting. The child died seven hours after admission, after a series of convulsions. Necropsy revealed evidence of congenital heart disease and an abscess in the left parieto-occipital region. The abscess contained, besides streptococci with alpha hemolysis, obvious oral organisms, namely, fusiform bacilli and spirochetes. No path of extension from the oral cavity to the brain and no recognizable origin for infected emboli could be found.

The second case was that of a 19 year old Negro woman who had had several previous admissions to the hospital. She had syphilis and was also diabetic. She entered the hospital with acute glossitis. During treatment for her infection and diabetes left-sided seizures developed, with a residual left hemiparesis and coma. The spinal fluid showed evidence of infection, culture revealing an atypical streptococcus with alpha to gamma hemolysis. Blood cultures repeatedly failed to yield any organism. The suddenness and the dramatic character of the onset led clinical observers to the conclusion either that a cerebral embolism, primary site unknown, had developed or that there was an intravascular thrombosis. The possibility of a brain abscess was apparently not considered. Although no obvious focus for the origin of the septic emboli could be found either clinically or pathologically, the infections of the mouth and lungs must both be considered as possible points of origin. Autopsy revealed an abscess of the right parieto-occipital area, which communicated with the lateral ventricle. The heart exhibited multiple congenital defects.

The third case was that of a 20 year old white woman who was known to have had congenital heart disease. Two weeks prior to admission she began to experience intermittent headaches, which became constant four days before she entered the hospital. The headaches were accompanied with nausea and projectile vomiting. Although she believed that she had had some fever, she experienced no chills. She had clinical and laboratory evidence of meningitis. However, it should be noted that at no time did a culture of the spinal fluid reveal organisms, although on one occasion gram-negative cocci were reported to have been seen on smear. The patient died twenty-four hours after admission to the hospital. At autopsy the only pertinent observations related to the heart and brain. The tetralogy of Fallot was present. In the brain there was a small abscess in the left superior temporal convolution. At one point the abscess communicated with the lateral ventricle in the subarachnoid space. As in the previous case, the underlying brain abscess was entirely unsuspected.

Three cases of cerebral abscess complicating congenital septal defects of the heart are added to those previously reported, bringing the total number of such cases in the literature to 26. In only 3 cases in the literature has an antemortem diagnosis of the disease been made and surgical drainage been instituted, a proportion which reflects principally the difficulty in diagnosis, arising in most instances from unfamiliarity with this complication of septal defects of the heart.

With the increased number of cases reported, it is to be hoped that in cases of congenital heart disease, especially those with the tetralogy of Fallot, underlying brain abscess will be considered in the diagnosis of any focal neurologic damage or meningitis. Certainly, only early recognition will permit successful surgical intervention and hope for cure of this uncommon syndrome.

GUTTMAN, Philadelphia.

AMBLYOPIA RESULTING FROM HEMORRHAGE. RONALD A. COX, Arch. Ophth. **32:** 368 (Nov.) 1944.

Occasionally after profuse distant hemorrhage there is noticed immediately, or, more frequently, after the lapse of days, a sudden diminution of vision, which often goes on to complete and permanent blindness, with the ophthalmoscopic picture of atrophy of the optic nerves. Many theories as to the pathogenesis of the condition have been offered. Von Graefe specifically assumed that hemorrhage into the optic nerve sheaths was the cause. Westhoff and Ziegler stated the belief that the loss of vision was due to primary fatty degeneration of the optic nerve induced by ischemia. Hoffman attributed the amblyopia and subsequent atrophy of the optic nerve to retrobulbar neuritis. Leber stated that the ocular changes were produced not only by direct loss of blood but also by retardation of the circulation, which resulted in edema and multiple hemorrhages in the retina. Goerlitz ascribed the condition to foci of degeneration, probably of thrombotic origin, behind the lamina cribrosa. Wolff stated that this type of amblyopia was due to spasm of the arteries, resulting from lack of oxygen. Moore, in discussing Wolff's paper, suggested that the unilaterality observable in some cases indicated a greater tendency to vascular spasm on one side of the body than on the other, such as occurs in migraine. Hartmann and Parfonry stated that the efficacy of vasodilator therapy indicated that vasoconstriction was the cause of the amblyopia. Groenouw asserted that persons who present amblyopia after hemorrhage have previously been ill and that a latent toxin manifests its effect by producing blindness immediately after the hemorrhage. Holden stated that the process is peripheral and that the cause must lie in some product formed in the restoration of lost blood which is toxic under certain conditions. Duggan stated that the toxin responsible for the amblyopia following hemorrhage is a vasoconstrictor.

Regardless of specific pathogenesis, deprivation of blood if sufficiently prolonged will cause loss or impairment of function. The case which the author reports was one of severe hemorrhage following a serious trauma.

SPAETH, Philadelphia.

"VIBRATION SENSE" AS A DIFFERENTIAL DIAGNOSTIC SIGN IN DOUBTFUL CASES OF PARKINSONIAN SYNDROME. ALFRED GORDON, J. Nerv. & Ment. Dis. **101:** 589 (June) 1945.

In cases of unilateral parkinsonism, such as is seen after cerebral trauma, there is frequently ground for diagnostic doubt, and in these instances Gordon has found that hypersensitivity to the oscillations of the tuning fork is present on the affected side. The test is especially useful in differentiating parkinsonism from hysteria, and the author suggests that it may have medicolegal value.

CHODOFF, Langley Field, Va.

RELATONSHIP OF INTRACRANIAL PRESSURE AND PRESENCE OF BLOOD IN THE CEREBROSPINAL FLUID TO THE OCCURRENCE OF HEADACHES IN PATIENTS WITH INJURIES TO THE HEAD. A. P. FRIEDMAN and H. H. MERRITT, J. Nerv. & Ment. Dis. **102:**1 (July) 1945.

Friedman and Merritt report data concerning the cerebrospinal fluid pressure and the presence of blood in the cerebrospinal fluid immediately following injury in 265 patients with acute head trauma and correlate their findings with the occurrence of headaches for periods varying from two to twelve months after the injury. The pressure was less than 160 mm. in 56 per cent of patients, 160 to 200 mm. in 22 per cent, 200 to 250 mm. in 17 per cent and over 250 mm. in 5 per cent, while the cerebrospinal fluid was clear in 65 per cent and bloody in 33 per cent. There was a high degree of correlation between abnormalities of the cerebrospinal fluids of either type and the duration of coma and amnesia after injury. In general, the number of headaches, in either the immediate or the late posttraumatic period, did not vary significantly in patients with and without abnormalities of the spinal fluid.

CHODOFF, Langley Field, Va.

MACROSTEREOGNOSIA. L. HALPERN, J. Nerv. & Ment. Dis. **102**:260 (Sept.) 1945.

Halpern reports a new phenomenon which he terms macrostereognosis in the case of a 47 year old man who displayed the sudden onset of dizziness and a sensation as though his right arm had been electrified. Neurologic examination revealed left-sided hemihypesthesia with preservation of deep sensation, astereognosis and loss of position sense of the right hand; right-sided hemiparesis, and nystagmus on lateral gaze. About six weeks later he experienced a "freezing" sensation, together with severe, spontaneous painful sensations over the left half of the body. This suggested a lesion of the right thalamus with probable involvement of the left thalamus as well. The right-sided astereognosis gradually regressed, but as it did the following phenomenon appeared: Although the patient was able to recognize objects placed in his right hand, they appeared bulkier and more massive than they did when placed in the left hand. This abnormal perception was not limited to the hand but involved the entire right half of the body. After about a month it gradually disappeared, first from the trunk and then from the hand and fingers, persisting longest in the first three fingers.

Macrostereognosis is explained as a sensory irritation phenomenon and as an example of the "paradox of contrasting effects," which is characteristic of thalamic disorders. It bears an analogy to the already known macropsia, which has been regarded as an isolated occurrence in the pathologic picture of sensory perceptions.

CHODOFF, Langley Field, Va.

FACTORS INFLUENCING MORTALITY IN HEAD INJURY. HAROLD C. VORIS, Radiology **44**:166 (Feb.) 1945.

Voris reports on an analysis of 2,714 cases of head injury, the total mortality in which was 11 per cent.

The severity of the injury was the most important factor in the prognosis. The age of the patient was equally important; from the age of 40 the mortality increased steadily.

Too much significance should not be attached to the presence of fracture. Although cases of fracture showed a mortality of 16.5 per cent, as compared with a mortality of 9.3 per cent in cases of nonfracture, fracture was present in only 56.7 per cent of the 120 cases of deaths. It is, therefore, not necessary to have immediate roentgenograms of the skull unless depressed fracture, a penetrating wound of the cranial cavity, middle meningeal hemorrhage or fracture involving the nasal sinuses is suspected.

A bloody spinal fluid worsens the prognosis (17 per cent mortality, as against 6.7 per cent mortality with clear spinal fluid), since severe cerebral contusion or laceration is probably present.

A spinal fluid pressure above 140 mm. of water carries a graver prognosis (21.5 per cent mortality, as against 6.7 per cent with normal pressure).

Associated injuries of the chest, spine or spinal cord definitely raise the mortality rate. This is also true of preexisting chronic cardiovascular and renal disease.

Acute medical complications are additional factors in influencing the mortality. Thus, of 120 fatal cases, pulmonary complications occurred in 18.3 per cent, meningitis in 5.7 per cent and acute cardiovascular renal complications in 7.5 per cent.

In the entire series, there were 20 cases of meningitis, with a mortality of 60 per cent. Treatment consisted essentially in administration of large doses of sulfadiazine until the cell count was normal and the culture was sterile. Sulfadiazine was also administered prophylactically to patients with bleeding or with drainage of spinal fluid from the nose or ear.

TEPLICK, Washington, D. C.

TUMORS OF THE THIRD VENTRICLE. RAFAEL J. BABBINI, RAUL BARCELONE and JUAN B. ALBERTENGO, Rev. argent. de neurol. y psiquiat. **9**:207 (June) 1944.

The authors report 6 cases of tumor of the third ventricle, in 2 of which the diagnosis was not verified. There were 2 cases of colloid cyst of the third ventricle, 1 of teratoma and 1 of ependymoma. They emphasize the value of iodoventriculography in the diagnosis of tumors of the third ventricle. In none of the 4 verified cases did recovery occur, in spite of operation. In 2 cases there was paralysis of upward gaze. An unusual feature was a history of epileptic attacks for a few months in a case of colloid cyst of the third ventricle. In 2 cases papilledema was not present, in spite of evident obstruction of the aqueduct of Sylvius. In 2 cases of ependymoma and colloid cyst, there was a long history of bouts of headache, of approximately twenty years' duration. In a nonverified case the ventriculogram showed a tumor of the third ventricle. The patient improved after a rubber tube was inserted to drain the lateral ventricle into the cisterna magna.

SAVITSKY, New York.

Encephalography, Ventriculography, Roentgenography

ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS PREREQUISITE TO DIAGNOSIS OF BACK TRAUMA. EBEN J. CAREY, Radiology **41**:554 (Dec.) 1943.

Slight trauma may disable vertebral bodies which have been repeatedly insulted by postural errors and mechanical strain. The average length of the spinal column is 70 cm., about one-fourth the length being made up of intervertebral disks. The primary curves, persisting from the embryonic axis, are those of the dorsal and the sacral areas. The cervical and lumbar curves are secondary, or accommodation, curves. The lumbar curve appears when the child begins to stand and walk. Physiologic scoliosis, with convexity to the right, is present in the upper dorsal region in right-handed persons.

Persons with anomalies of the spinal column have less stable backs and are more susceptible to trauma. An elongated transverse process of the fifth lumbar vertebra, found in 25 per cent of persons with pain in the lower part of the back, impinges on the ilium and may form a painful bursa. Sacralization of the fifth lumbar vertebra, normally seen in 3.5 per cent of persons, occurs in 50 per cent of patients with pain in the lower part of the back. Defects in the neural arch, "kissing" spinous processes, abnormal lumbar lordosis, spondylolisthesis and constitutional variations of body build, all predispose to back sprain.

TEPLICK, Philadelphia.

DIFFERENTIAL DIAGNOSIS OF TRAUMATIC LESIONS OF THE SPINE. S. A. MORTON, Radiology **41**:560 (Dec.) 1943.

Morton discusses several conditions of obscure origin which might be concluded on roentgenologic grounds to be the result of a definite injury, but which are probably not of traumatic origin.

Nontraumatic dislocation of the atlantoaxial joint occurs in young persons, accompanying infections of the throat or cervical nodes. It may occur with rheumatic fever. The dislocation is rotary, and usually roentgenograms reveal a definite separation between the odontoid process and the anterior arch of the atlas. Hypertrophic changes of the posterior margins of the cervical vertebrae, with projecting spurs, may produce nuchal pain, radiating down the arms. Oblique views aid in visualizing this condition. Senile osteoporosis, without trauma, may produce a vertebral collapse in the dorsal area. A previous trauma cannot, however, be entirely disregarded.

Scheuermann's disease, or osteochondrosis of the secondary vertebral epiphyses, is fairly common. The characteristic roentgenographic appearance of irregular, wavy upper and lower surfaces of the body, with symmetric wedging, does not

suggest the effects of fracture. Localized epiphysitis, in the lower dorsal or upper lumbar vertebra, occurs in an anterior corner of the body. Increased density, fragmentation and beveling of the vertebral body occurs characteristically. The body of only one vertebra is involved. "Persistent epiphyses," a defect in the upper anterior border of a vertebral body, with a triangular piece of bone above and slightly anterior, is asymptomatic. The cause is unknown. Nuclear molding, or Schmorl's nodes, is a biconcave expansion of the intervertebral disks, seen most commonly in the lumbar area. They are unrelated to injury. Kümmell's disease (compression fracture of a vertebra), a post-traumatic rarefaction and collapse of a vertebral body after a latent period, is not an entity established beyond doubt.

TEPLICK, Philadelphia.

OSTEOPOROSIS CIRCUMSCRIPTA CRANII. FRANK WINDHOLZ, Radiology **44**:14 (Jan.) 1945.

Windholz reports 3 cases of this condition in none of which the disorders was related to Paget's disease. Case 1 was that of a woman aged 63, and the osteoporosis was part of a well recognized leontiasis ossea, as proved by biopsy. Case 2 concerned a woman aged 58 in whom the osteoporosis was associated with a peculiar osseous condition of the skull present since youth, called fibrous osteodystrophy and appearing clinically as leontiasis. Extensive hyperostoses surrounded the osteoporotic areas. Case 3, that of a woman aged 58, showed the changes in the skull characteristic of osteoporosis circumscripta, with atypical roentgenographic and clinical signs suggestive of hyperparathyroid disease. A few years later the latter diagnosis was firmly established, both clinically and roentgenographically. A parathyroid adenoma was removed.

In the literature, only 60 per cent of the cases of osteoporosis circumscripta were related to Paget's disease. Other associated conditions were leontiasis ossea, bony tumors of the jaw, hyperparathyroidism and tumors of the brain. The author believes that osteoporosis circumscripta is a characteristic reaction of the bones of the cranium and is probably caused by circulatory disturbances in the presence of bony hyperplasias or of bony tumors near the base of the skull.

TEPLICK, Washington, D. C.

INTRACRANIAL ANGIOGRAPHY. C. F. LIST, C. H. BURGE and F. HODGES, Radiology **45**:1 (July) 1945.

Intracranial angiography offers a means of obtaining information of value in cases of suspected intracranial aneurysm and anomalies of intracranial vessels, in certain cases of arterial occlusion and in cases of expanding lesions involving one cerebral hemisphere which have not been accurately localized.

The internal carotid artery supplies intracranial branches to the structures above the tentorium, while the subtentorial portions of the brain are supplied by branches of the vertebral vessels.

For carotid injections, local anesthesia is used, and the common carotid artery is exposed. Whenever feasible, injection is made into the internal carotid artery directly. When the common carotid artery must be used, the external carotid artery is occluded during the injection.

Ordinarily, three injections are made, two to obtain stereoscopic lateral exposures, and the third for a posteroanterior view. The opaque material is forced into the artery as rapidly as possible. When the injection is about two-thirds complete, the first lateral exposure is made. As soon as the film can be changed (about three seconds), a second lateral roentgenogram is made, which records venous return. After irrigation with isotonic solution of three chlorides U. S. P., the entire procedure is repeated, with the roentgenographic tube shifted for stereoscopic pictures. During the third injection a single posteroanterior exposure is made.

Exposure of the vertebral artery for direct injection is technically difficult. If the vessel is satisfactorily exposed, a direct puncture may be made at the level of the sixth cervical body; retrograde injection into the subclavian artery will indirectly fill the vertebral vessel and its branches.

Despite its radioactivity, a 25 per cent colloid suspension of thorium dioxide in amounts not exceeding 30 cc. is the preferred injection medium, giving the best visualization and being virtually nonirritating. The authors believe 30 cc. or less is probably without late harmful effects from radioactivity.

TEPLICK, Washington, D. C.

OSTEOGENIC SARCOMA OF THE SKULL. L. H. GARLAND, Radiology **45**:45 (July) 1945.

While secondary sarcomatous degeneration in Paget's disease (osteitis deformans) of the skull is not uncommon, primary osteogenic sarcoma of the skull is extremely rare. The former occurs in persons of the older age groups, when primary osteogenic sarcoma of any bone is unlikely.

A seaman, aged 17, noticed a lump at the base of the skull, which had grown in two months to the size of a ping-pong ball. It caused some limitation of cranial movement and was slightly painful. At a Pacific base hospital a diagnosis of osteochrondroma was made and the mass removed. No report of biopsy was available. In about eight weeks the mass recurred, being slightly more painful and reaching about 8 cm. in diameter. Roentgenograms of the skull showed extensive thickening of the outer table of the occipital bone, chiefly to the right of the midline, with considerable spiculation and a small amount of irregular calcification in the tumor. The inner table appeared completely normal. A roentgenographic diagnosis of primary osteogenic sarcoma of the occipital bone was made.

The tumor, together with invaded soft tissues and muscles, was excised, and a molded tantalum plate was inserted to replace the bone. The histologic diagnosis was sarcoma, osteoblastic and osteogenic. Despite intensive postoperative irradiation and the excellent condition of the patient one month after irradiation, the outlook was considered hopeless.

TEPLICK, Washington, D. C.

Congenital Anomalies

AN UNUSUAL FAMILIAL SYNDROME. A. P. FRIEDMAN and J. E. ROY, J. Nerv. & Ment. Dis. **99**:42 (Jan.) 1944.

Friedman and Roy report on a family of 6 feebleminded children of parents of average intelligence. Each had a mental age of less than 3 years and presented identical neurologic signs; namely, strabismus, extensor plantar reflexes, speech defect and foot deformity. The parents were cousins, their fathers having been half-brothers. Electroencephalograms of the mother and of all 6 siblings showed a uniform tendency toward high voltage and irregular frequency.

CHODOFF, Langley Field, Va.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Madelaine R. Brown, M.D., *Presiding*

Regular Meeting, April 26, 1945

Clinical Implications of the Bellevue-Wechsler Test, with Particular Reference to Cases of Injury to the Brain. DR. MILTON GREENBLATT, MISS ROSALINE GOLDMAN and DR. GAYLORD P. COON.

Experience with the Bellevue-Wechsler test at the Boston Psychopathic Hospital over a period of six years leads us to believe that it is a superior test because it can be administered with relative ease, has been standardized on adults over a wide age range, has the flexibility of a point scale, with the possibility of direct comparison of performance on various test items, and taps a wide range of functions and elicits data of considerable value and interest to the clinician. In cases of the state characterized by the term "brain damage," this test would seem of special value for both diagnosis and investigation.

Two types of signs were found in cases of damage to the brain—quantitative and qualitative. The quantitative signs consisted essentially in a wide discrepancy in the weighted scores of various subtest items. As a rule, performance on nonverbal items (picture arrangement, picture completion and block designs) was most seriously affected, but there was always at least one verbal subtest in which there was loss of ability to function. The qualitative signs were best displayed in the nonverbal test items, in which the patients showed rigidity, inability to shift attention or change the mode of response, inability to ignore superficial or extraneous stimuli and difficulty in organizing material into either a required pattern (block designs) or a meaningful, logical sequence (picture arrangement). In cases in which both quantitative and qualitative irregularities of performance were found, clinical analysis revealed a high incidence of damage to the brain.

Within the broader framework of the "organic" pattern as elicited with the Bellevue-Wechsler test, we noted seven variant configurations, or profiles, which were more or less mutually exclusive. The full significance of these profiles is not yet clear; certainly, they are not specific for any given disease entity. As a rule, the greater the loss of function as displayed in the psychologic examination, the more serious was the cerebral damage. There were suggestive relationships between the particular psychologic configurations and certain groups of symptoms, but the meaning of these trends must await a greater accumulation of cases.

DISCUSSION

DR. FREDERICK WYATT: Of the criticism which traditionally is expected to follow a scientific presentation, I have little to offer. This is an interesting and, from the standpoint of the psychologist at least, a rather successful study. It may have been a surprise that we were not presented with more statistics. Remembering the folkways of psychologists, we might have anticipated blackboards full of figures and tables. The authors should be commended for having emphasized the qualitative aspects of their observations. No quantitative study should be attempted until the possibilities of organizing the material in one's thought and of establishing a tentative framework of reference have been exhausted. To test the most sensible hypothesis is the function of statistics in an investigation like the present one. As I have had a previous opportunity to discuss this paper, I shall sum up its quantitative aspects by saying that the authors might now find it

helpful to apply χ_2 technics systematically in order to obtain measures of the differential significance of individual results.

In 72 per cent of the cases the clinical and psychologic findings were in agreement. The remaining 28 per cent present a problem. How can one account for this disagreement? First, it should not be forgotten that this study grew out of routine clinical work. Patients do not care to take tests; they are full of wiles and offer complex problems for psychologic study, to which I shall return in a moment. The medicoclinical work-up was not always so complete as one would have desired. If one had for all the subjects data from all the clinical tests given to a number of them, the percentage of agreement between clinical and psychologic diagnosis might well have been higher.

In order to evaluate the significance of the 28 per cent disagreement between the two methods, with the diagnosis of "brain damage" by psychologic methods unsupported by medical ones, one must ask oneself what it actually means when psychologists report findings such as those presented here. Primarily, it means only that the subject under scrutiny shows deficiencies in certain types of intellectual action, or in certain aspects and functions of his thinking. In psychologic testing, certain patterns of deficiency were found empirically to concur with the clinically established diagnosis of cerebral damage. On a somewhat more deductive line of reasoning, these deficiencies also seemed to indicate that with impairment of intellectual functions one would expect to encounter inadequate functioning of the brain. This last point, however, while indicating that a brain cannot function at "normal" capacity when operating in such a deficient manner,, does not necessarily imply that this inferior performance is due to one of the stark pathologic processes clinically labeled "brain disease."

In accordance with Dr. Goldstein's ideas, the aspect of thinking most conspicuously reduced in these cases is the ability to perform abstractions. One might elaborate and add that there is reduction in the ability to analyze a whole or to synthesize parts into a whole, to draw simple inferences from data, to recognize configurations and to fit elements into them correctly, to learn, to retain and to recall from memory. Besides actual cerebral disease, at least two other factors may account for a reduction in at least some of these functions: congenital inferiority, as in feeblemindedness and probably in some forms of psychopathic personality, and states of emotional conflict causing conditional and temporary disabilities of a somewhat different kind. While the more clearcut of these disturbances can be distinguished rather successfully with the Wechsler-Bellevue test, one need only recall the infinite complexity of psychologic qualities, the fusion and overlaying of character traits and disease syndromes which is the rule, rather than the exception, in our clinical material, to acknowledge that in the 28 per cent the negative clinical diagnosis might be final and the psychologist's statement of an impairment of thinking might still be correct, though it may not spell "brain disease" in the succinct sense of the clinic.

The pattern analysis presented by the authors seems to me a successful step toward further isolating and clarifying the various subpatterns of deficient intellectual functioning and of approximating their clinical meaning. Would it be possible now to go further and to aim toward a more detailed analysis of patterns of performance? If two patterns of test performance are too vaguely similar to be distinguished, yet do not accord at all with corresponding clinical findings, one must assume that there are factors of difference in the results not yet seized on. Could one map out in detail all the mental functions called forth in each of the subtests of the Bellevue scale? Some of the subtests seem to be based on memory and recall only; most are more complex, however. The cube test, for instance, the most sensitive of the Bellevue subtests, involves abstraction, generalization, analysis, synthetic acts and probably more. Could a list of intellectual functions be designed into which a subject's performance could be entered, in terms not of subtest scores but of abilities and disabilities shown in performing these functions? Pattern analysis could thus be put on a much more differential basis. Several subgroups within the somewhat tenuous class of encephalopathic

performances might be isolated, and the test might thus be made a more sensitive instrument of diagnosis.

DR. KURT GOLDSTEIN: This is an interesting and clinically important paper. If I were to say anything, I should question whether it is necessary and useful to employ so many tests. One can often reach the same result in an easier way by careful analysis of the procedure of the patient in one test. That is the case particularly with damage of the function of abstraction. There is scarcely one test which could not be used for this purpose. It is only easier to find the defect with the tests I have proposed. There is an interesting difference in tests as to the amount of endowment the patient needs to fulfil the test and, on the other hand, as to the amount of impairment of some functions, particularly abstraction, which can be hidden by use of endowment. Always, analysis of the procedure by which the test is fulfilled is the most important point, sometimes with use of subtests which impede use of endowment.

DR. ANDRAS ANGYAL, Worcester, Mass.: This study demonstrates again the value of psychologic test procedures in neurology, particularly in cases in which cortical damage is suspected. In the diagnosis of cerebral damage the Wechsler-Bellevue test is of course not the test of choice. The test, having been devised primarily for a different purpose, includes many items which are not particularly helpful in the diagnosis of cerebral damage. There are, however, some other items in the test in which one is likely to obtain rather characteristic responses in the case of cortical damage. The authors made a contribution of significance in pointing out the characteristics in the results of the Wechsler-Bellevue test which suggest the diagnosis of cerebral damage; the test is being given routinely in many psychiatric hospitals, and it is an advantage to be able to derive useful information in addition to determination of the intelligence level.

DR. LEO BERMAN: I am interested in the cases of functional disorders included in the study. In what percentage of these cases would you find organic damage to such a degree that it would lead to a change in diagnosis from functional to organic disease?

MISS ROSALINE GOLDMAN: It should be emphasized that this whole study is the outgrowth of routine testing at the Boston Psychopathic Hospital. We are required to give psychologic examinations in court cases, and we have suspected cerebral damage in many instances. We feel that a routine psychologic examination gives a great deal of incidental information of great use to the clinician before it is available from other sources. When a psychologist is primarily interested in studying cerebral damage, he will use other tests especially designed for that purpose.

DR. MILTON GREENBLATT: Concerning the 28 per cent of "problem" cases to which Dr. Wyatt referred, I can say that the psychometric test shows no less loss of function in this group than in the group in which clinical corroboration was found. Psychologically, the defects in the 72 per cent group and those in the 28 per cent group were roughly the same. There was no difference in age distribution; so age was not a factor. We did get the impression that the 28 per cent group was worked up less completely than the 72 per cent group. Why were these cases not worked up as well? Probably largely because the indications were not there. If we had tested specifically for cerebral damage, instead of carrying out routine tests, we probably would have found many cases of the 28 per cent group that would fall into the 72 per cent group, thus enlarging the latter. As Dr. Angyal mentioned, and in reply to Dr. Goldstein's question: This was a routine test and gave data besides those relating to cerebral damage. We wondered how much weight the clinical staff should put on the observations of the psychologists. In 72 per cent of the cases in which the psychologists offered the diagnosis of cerebral damage there was some clinical corroboration. How often is there clinical evidence of damage to the brain when the psychologists say nothing is wrong? We have found it occasionally, but the percentage is very low.

We have not yet analyzed any large series of cases in which the diagnosis was manic-depressive psychosis or schizophrenia. In how many of such cases will these abnormal psychologic responses be found? I agree with Dr. Wyatt that the absence of complete overlap of clinical and psychometric data leaves room for speculation. One may ask the cause of the psychologic disorder found in the 28 per cent group. Factors of endowment and constitutional factors cannot be ruled out. In Wechsler's series taken from the population at large, from which he derives averages which one relies on, in what percentage did these abnormal responses occur? Dr. Goldstein's writings and observations have meant a great deal to us. They have provided significant leads for our psychologists. Whenever in the routine Bellevue test we found suggestive evidence of cerebral damage, we continued our study with the aid of more specific tests, such as those devised by Dr. Goldstein.

Fatigue in Relation to Adrenal Cortex. Dr. Gregory Pincus and Dr. Hudson Hoagland, Worcester, Mass.

Studies of stress in relation to the output of 17-keto steroids as a measure of the activity of the adrenal cortex were reported, and the effect of administration of certain steroids on fatigue of psychomotor performance was described. The output of 17-keto steroids in psychotic patients and in controls under conditions of stress was also compared.

In the first series of studies, 7 college students were given 67 two to six hour runs, after an adequate learning period, on a serial coordination meter with airplane type controls.

Timed samples of urine were collected before each run and also for the period of the run. After correction for time of day from a curve for the diurnal excretion rhythm, the output of 17-keto steroids under stress, i. e., the mean test value for 17-keto steroids minus the control value, expressed as milligrams excreted per unit of time, was calculated. This value for excretion of 17-keto steroids under stress was found to be correlated to a striking degree with the subject's ability to avoid errors due to increasing fatigue, in that the men showing the lowest output of 17-keto steroids under stress had the fewest errors.

In another series of experiments on an airplane type pursuit meter, anoxia was found to increase the over-all output of 17-keto steroids, in close relation to failure in scoring ability. The output of 17-keto steroids under stress was studied in 16 Army pilots in 152 routine instruction flights and in 7 Pratt and Whitney pilots in 56 test flights. Correlation coefficients of $> 0.95 \pm < 0.01$ were found between the per cent of time the pilot was airborne and his output of 17-keto steroids under stress. An independent rating of the fatigability of Army fliers made by their squadron commander correlated significantly with the degree of diuresis during stress.

Attempts were made to find a steroid substance that could be taken orally and that would enhance performance in fatiguing psychomotor operations and which, at the same time, would be harmless.

In a preliminary series of tests, neither oral administration of adrenal cortex extract nor injections of progesterone were accompanied with improvement in pursuit meter scoring, but the administration of Δ^5-pregnenolone was effective. Seven Army pilots accordingly made a series of scored runs on an airplane type pursuit meter and were given alternately placebos and Δ^5-pregnenolone (50 mg. per day), followed by placebos again. A significant improvement in scoring—in absolute score, in decrement measures and in "emergency" performance—occurred during the administration of pregnenolone. These findings were subsequently confirmed by a series of tests on 7 hired civilian subjects, who, although their performance improved with pregnenolone, showed much less improvement than the aviators. In all, 304 tests were made with the 14 men. Those persons under most

stress from their daily work, provided they were striving to make maximum pursuit meter scores, were the ones whose performance improved with pregnenolone. In another series of tests on psychotic patients and on indifferent hospital employees we found no improvement with pregnenolone. These groups was characterized by low incentive and low effort in the tests.

The effect of pregnenolone on industrial production was then studied, and the following observations were reported:

Eight leather cutters were studied over a period of eight weeks. The men received no incentive pay, and the amount of production per se was therefore not a measure of the effects of experimental procedures. The wastage of leather was measured and compared when the men were receiving 45 mg. of Δ^5-pregnenolone per day and when they were receiving placebos indistinguishable from the pregnenolone pills. Administration of pregnenolone was not found to lessen the wastage in cutting sole leather.

Twelve turret lathe operators (8 men and 4 women) were studied in relation to their daily production of bayonets on a piece work incentive basis when they were receiving pregnenolone and when they were receiving placebos. During administration of the placebos the efficiency of production increased 10.1 ± 2.18 per cent; during administration of pregnenolone the increase was 18.3 ± 1.71 per cent. The difference of 8.2 per cent is three times the standard deviation, and the value of P is 0.005. The difference is therefore statistically significant.

The number of scrapped bayonets was less by 32.7 per cent when the workers were receiving pregnenolone than when they were receiving placebos, but this difference in figures for scrapped production is not quite statistically significant (P-0.06).

On discontinuation of all medication, an increase in efficiency of about 10 per cent remained during the four weeks the production was continued. The role of job stress and incentive was discussed in relation to the findings.

Piece work production of 173 male and female workers making optical goods was studied when they were receiving placebos and when they were receiving pregnenolone. A significance increase of 4.2 per cent in over-all production was found for 77 workers taking 50 mg. of Δ^5-pregnenolone per day as compared with their previous production levels. This was 1.3 per cent higher than the levels when they were taking placebos, and the difference is statistically significant.

The decrease in wastage and repairs for 39 workers amounted to 18.9 per cent when they were taking pregnenolone and 13.7 per cent when they were taking placebos as compared with their preexperimental levels.

Ninety-six workers were studied for three months. One-third took 70 mg. of Δ^5-pregnenolone per day in the form of pills; another third took 25 mg. per day and a third took 0.1 mg. per day (a placebo for all practical purposes). The group receiving 70 mg. of pregnenolone showed most pronounced improvement in earnings and in the saving of wastage. The improvement shown by the group receiving 25 mg. a day fell between that of the group receiving 70 mg. and that of the group receiving 0.1 mg. a day. There were thus demonstrated significant differences in dosage in relation to improvement of industrial production resulting from the ingestion of pregnenolone.

Some improvement of production due to pregnenolone tended to be retained after the termination of medication.

A comparison of function of the adrenal cortex in normal and in psychopathic subjects under the stresses of cold, heat, pursuit meter operation and psychologic tests revealed the following facts:

1. A rise in urinary 17-keto steroids during stress, followed by a sharp fall after stress, occurred in normal men; this pattern was not observed in most psychotic subjects.

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These data are interpreted as indicating a failure in response of the adrenal cortex to stress in psychotic men.

DISCUSSION

DR. JOSEPH C. AUB: This is obviously important work. It reminds me of Professor Benedict's studies of fatigue in student examinations. He concluded that it took 2 peanuts' worth of calories to cerebrate actively; that did not explain the fatigue of an hour's examination. This study comes near explaining the fatigue that comes with hard work. It is surprising that the adrenal glands should be so greatly involved. When Selye first described the alarm reaction, I was skeptical about it. One cannot be skeptical about it any more. The point which puzzled me was the prolongation of the immediate rise in excretion of 17-keto steroids with alarm and the production of these substances for weeks afterward. The authors have not shown the speed of recovery of ketosteroids after alarm, if one could call it that—the acute stresses they have been studying. How long is the rate of excretion of 17-keto steroids distorted?

I have nothing new to offer in regard to this work. The only work analogous is that on the deer. My colleagues and I have been studying the growth of deer antlers and the action of 17-keto steroids. We tried to determine the excretion rates but failed. I am interested in the extraordinary psychologic reactions of the deer to injections of the steroids. We have used only testosterone. The deer is a wonderful animal for psychologic study. The male is like the female ten months of the year. He is charming and has none of the unpleasant male characteristics. Then for two months the buck has all the disagreeable characteristics usually manifested by man. He is aggressive and irritable. If one gives a buck testosterone when he is doelike (we wanted to see what the drug would do to the antlers), he becomes like a male. He has all the unpleasant characteristics. One cannot get into the cage with him without being attacked. He is aggressive toward the doe, although it is not the season. He tries to fight; he tears his antlers. If testosterone is injected two months before the antlers start to grow, he shows the same characteristics he would later. A few years ago I talked to this society about the lack of effect of 17-keto steroids and estrogen on the characteristics of maleness and femaleness. The rates of excretion of these substances were the same in girls and boys. Therefore the characteristics of sex were not explained by their rates of excretion. One does change the personality of a buck by the injection of testosterone. It is a potent hormone.

DR. O. H. PEARSON: I am not qualified to talk about this subject. My associates and I have taken considerable interest in it, but, unfortunately, we have nothing to report as yet. One phase of the work of Hoagland and Pincus is the use of drugs and the measurement of their effect. I should like to ask what hormonal activity pregnenolone has. It was interesting to note the curves in the measurement of piece work of the subjects, to note that the work increased with administration of placebos. One finds that in all clinical work on drugs, particularly when the exact action of the drug is not known.

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DR. JOSEPH C. AUB: Does it make any difference in the action on the sympathetic nervous system whether the stress situation is pleasant or unpleasant?

DR. HUDSON HOAGLAND, Worcester, Mass.: In reply to Dr. Finesinger, we have not found out much about one stress as compared with another. We have used various stresses to determine the hormonal involvement. In students taking examinations, for example, we observed the ketosteroid response to stress. Such stress may be comparable to pursuit meter operation and exposure in a cold room, but we cannot compare its strength. We have used the pursuit meter under conditions of anoxia. We have found that the lymphocyte count falls, just as it does in a hot room. We have not been able to compare one stress with another, except to note that extremely varied stresses seem to make for changes in the output of ketosteroids.

DR. GREGORY PINCUS, Worcester, Mass.: To answer Dr. Aub's question first: We have not measured accurately the latent period between stress and return to normal excretion. It would seem in the case of the pursuit meter operation that the effect in a normal person lasts a minimum of two hours. Every one of our poststress ketosteroid measurements represent a period of at least two hours, and the values are lower than one would expect if no stress had occurred. We have measured the lymphocyte response much more exactly. It is over in one or two hours after a stress applied for one hour. The 17-keto steroids represent an accumulation of metabolites of adrenal cortex hormones. The decrease in lymphocytes represents the action of active hormones of the adrenal cortex, according to White and Doherty: If the adrenal cortex extract is injected, the lymphocyte count drops; if normal animals are subjected to stress, it drops; if adrenalectomized animals are subjected to stress, it does not drop.

DR. JOSEPH C. AUB: Does it not seem strange that anything so essential as the adrenal cortex should exhaust itself and have a long latent period before it returns to function?

DR. GREGORY PINCUS, Worcester, Mass.: Do you call one or two hours long? If you refer to damage done due to burns, we have no experiments. We have only short time experiments. I should be interested in studying patients willing to live in a hot room longer. They might be more like the patients with burns. Why the depressed phase of 17-keto steroid output should continue so long in cases of severe damage is something which has not been answered by any experimentation I know of.

DR. HUDSON HOAGLAND, Worcester, Mass.: Mr. Fred Elmadgian is doing the stress work on rats. The stress consists in tying down the animal. After the rat has been tied down, the lymphocyte count falls for several hours. After that the count starts to rise; and in ten to fifteen hours it is nearly back to normal, even though the animal is still tied down. Animals with the adrenal glands removed do not show any drop in the lymphocyte count.

DR. GREGORY PINCUS, Worcester, Mass.: The effect of placebos is well known in industrial experimentation. Give workers anything and they do better. We were aware of this when we started the investigation; that is why we had the placebo controls. I do not know why placebos work.

Information is beginning to accumulate on the physiologic action of pregnenolone. Selye has shown that it has certain hormonal properties. It is unique among steroids in that in large enough doses it has a multiplicity of hormonal properties. It acts, for example, as an adrenal cortex steroid and as a progestin. It seems to be pharmacologically, as well as hormonally, active. Selye's notion, and one we have felt has some basis, is that it is a substance which might be converted in the body into hormonally active steroids. In subjects who have taken pregnenolone we find a striking increase in estrogen output in the urine. We find evidence for production of progesterone from pregnenolone in vivo. We do not know about conversion to adrenal cortex steroids. There is no doubt that pregnenolone is pharmacologically active in large doses. What we have used is probably a small dose for human subjects. We have not explored the limits of the dose. Perhaps we should try a wider range. There is, however, the matter of expense.

DR. HUDSON HOAGLAND, Worcester, Mass.: Torda and Wolff have reported that pregnenolone facilitates the synthesis of acetylcholine. Estrone and estradiol also do this, but these are the only three out of many steroids they have examined which are effective. One is tempted to speculate whether this factor may play a role in facilitating conduction in the nervous system in relation to fatigue.

Madelaine R. Brown, M.D., *Presiding*

Regular Meeting, May 17, 1945

Diagnostic Aspects of Unilateral Ruptured Cervical Disk. DR. JOST J. MICHELSEN and DR. WILLIAM JASON MIXTER.

The data to be presented were collected from 18 cases, in 5 of which lesions existed at the fifth, in 12 at the sixth and in 1 at the seventh interspace. In 12 cases the left side was involved. The chief complaint was pain associated with paresthesias in the region of the scapula, arm and hand, of two weeks' to two years' duration. Remissions in cases of a long-standing condition were common. Two types of pain were observed. All patients described sharp, stabbing pain from the shoulder down to the arm, forearm and fingers; most of them also experienced a dull, gnawing ache, more or less constant, in certain parts of the extremity. The pain either gradually progressed downward to the distal parts of the extremity, beginning in the shoulder blade, or was present in the entire area of distribution from the start. Discomfort in the lower cervical region as an initial symptom was mentioned only infrequently. Paresthesias involved the fingers chiefly, and in a few instances the whole extremity or part of the arm as well. Coughing, sneezing and straining precipitated or aggravated the pain and paresthesias. In the majority of cases certain movements of the neck had the same effect. The type of the aggravating movements was not uniform.

The distribution of the pain and paresthesias in the arm and forearm seemed to form a characteristic pattern according to the level of the lesion; in the fingers it is variable. Lesions at the fifth cervical interspace with compression of the sixth cervical nerve root involved the anterolateral portion of the upper arm, the antecubital region and the radial aspect of the forearm, thumb or thumb and index finger, or the fingers might be spared; lesions at the sixth cervical interspace (seventh cervical nerve root) involved the posterolateral aspect of the upper arm, the olecranon and the dorsal aspect of the forearm, wrist, second finger, second and third fingers, or second, third and fourth fingers and all the finger tips. In 1 case all the fingers seemed to be affected first; later the index finger alone was affected. The patient with a rupture at the seventh cervical interspace (eighth cervical nerve root) had pain and paresthesias in the inner aspect of the upper arm and forearm and the little finger. The shoulder blade was implicated in all instances regardless of the level of the lesion. In 3 cases a burning pain was experienced in the leg on the side opposite that of the shoulder-arm syndrome. Weakness of the arm or of specific muscles, as well as fasciculations and atrophy, was reported frequently. In all but 1 case one or two major, and probably significant, injuries had been received some time prior to the onset of the disability.

The more common clinical signs were: (1) absence of cervical lordosis; (2) tilting of the head to the side opposite the lesion; (3) aggravation of symptoms by certain movements of the neck; (4) tenderness of the shoulder blade, supraclavicular area and lower cervical portion of the spine; (5) sensory disturbances in a "dermatome" distribution; (6) atrophy, fasciculations and weakness of certain muscles; (7) diminished arm reflexes on the side of the lesion, and (8) more active leg reflexes on the same side.

None of the patients presented all these changes. Electromyographic studies were made by Dr. Arthur Watkins and Dr. Mary Brazier in 10 cases. Compression of the seventh cervical nerve root produced spontaneous discharges most often from the triceps muscle, as well as from the deltoid, extensor carpi ulnaris, extensor carpi radialis, flexor carpi radialis and opponens pollicis muscles. Recently it was observed that the intensity of the discharge varied with different positions of the neck. The cerebrospinal fluid protein was definitely increased in 7 cases, normal in 7 cases and nearly normal in 4 cases. The lowest value, 18 mg. per hundred cubic centimeters, was found in the case with the largest disk fragment in the series. The dynamics were normal except in a case in which the patient was admitted with a history of long-standing pain in the shoulder and arm and recent paraplegia following a dental operation. Roentgenograms showed absence of cervical lordosis, degenerative changes in the lower cervical portion of the spine and narrowing of the fifth and sixth cervical interspaces. The narrowing of the interspace did not always correspond with the level of the lesion. Myelographic studies were performed in 17 cases. In 2 cases the oil could not be removed from the site of the injection. In the others a definite filling defect or arrest of the radiopaque medium was shown at the site of the ruptured disk. The contrast substance was removed according to the method of Kubik and Hampton.

In the majority of cases treatment had been previously carried out for such conditions as bursitis, neuritis, myofibrositis, arthritis and disease of the coronary arteries. Differentiation of the root compression syndrome and these entities is not usually difficult. As to the scalenus anticus syndrome, it is probably true that a ruptured cervical disk may produce spasm of the scalenus anticus muscle. There also may be relief of symptoms following section of this muscle, just as nonspecific surgical measures apparently were successfully used in the past for the treatment of ruptured lumbar disk. In certain instances the clinical differentiation of intraspinal root compression and extraspinal disease of certain components of the brachial plexus, of mechanical origin, will remain a difficult problem. However, ordinarily the combination of symptoms and signs in a case of ruptured cervical disk is such that extraspinal disease can be well ruled out. In doubtful cases myelographic studies will settle the question.

DISCUSSION

Col. William P. Van Wagenen, M. C., A. U. S.: This is a fascinating subject. Major Scoville has been more interested in this phase of the problem than I. He has seen almost all the patients at the Army hospital at which we are stationed.

I wish the authors would comment further on the differential diagnosis of the ruptured cervical disk, particularly with reference to the scalenus anticus syndrome.

What percentage of civilians with pain in the shoulder and pain radiating down the arm actually have ruptured cervical disks? In the Army it is very small. The number of cases of ruptured disk in persons of military age is not great. I suspect that the authors' patients are older; it would be interesting to know what age group they represent. There is a great deal of variation in the distribution of pain referable to the cervical nerve roots. My colleagues and I see that every day. The variations in the arrangement of the brachial plexus are enormous.

A comment by the authors on the surgical details of their approach and treatment would be of interest.

This study has been carefully carried out, and it has been a pleasure to listen to its presentation.

Major William B. Scoville, M. C., A. U. S.: I have been interested in this clinical entity since 1939, and with Colonel Spurling I published a report of the surgical treatment in 12 cases in 1943 (*Surg., Gynec. & Obst.* **78**:350 [April] 1944). I am in accord with Colonel Van Wagenen's statement that a cervical

ruptured disk is a rare surgical lesion, but I believe that it is a common clinical entity. In other words, the disability is mild and only occasionally warrants surgical intervention. Compression of the nerve roots at the lower cervical vertebral foramens accounts for most of the diagnoses of scalenus anticus syndrome, brachial neuralgia and other obscure neuralgic pains of the shoulder and arm. When roentgenograms reveal arthritic changes localized to one interspace, I believe that the probable diagnosis is a cervical ruptured disk rather than hypertrophic arthritis. The so-called hard disk is three times as common as the soft variety in the cervical region. The hard variety is characterized by absorption of the nucleus with narrowing of the interspace, localized bony proliferation into the intervertebral foramen and a hard transverse ridge formed by protrusion of the cartilaginous plate and concomitant changes in the bone.

The proportion of clinical cervical ruptured disks requiring operation is low—probably less than 10 per cent. In the authors' series it constituted 6 out of 40 cases. In the remainder of the cases the disability was mild. The ratio of operations for ruptured cervical disk to operations for ruptured lumbar disk ranges from 1 : 50 to 1 : 12, being 6 : 270 in the authors' series, 2 : 120 at Cushing General Hospital and 12 : 145 at the Walter Reed General Hospital.

Diagnosis: In all cases in the authors' series, the lesion was located in the fifth or the sixth interspace. The signs and symptoms include stiffness of the neck; pain in the shoulder, radiating down the arm to the thumb and forefinger; weakness of grip and of function of the triceps and biceps, with corresponding loss of reflexes; subjective numbness of the index finger or the thumb; positive reaction to the neck compression test; tenderness over the adjacent spinous process, and increase of pain on coughing and sneezing. Vasomotor signs and ulnar distribution of the pain favor a diagnosis of scalenus anticus syndrome. As pointed out by Michelsen and by Spurling and Scoville, spasm of the scalenus muscle may be a prelude to cervical ruptured disk, but the pain soon shifts from an ulnar to a radial nerve distribution.

Myelographic examination, using 6 cc. of Pantopaque (iodized poppyseed oil, with special cohesive properties) and then removing it, should be done in all operative cases. A single Bucky film is generally sufficient to show the entire lower cervical dura and root sleeves. Roentgenographic diagnosis of a cervical ruptured disk is made on the basis of (*a*) narrowing of the intervertebral space, (*b*) bony proliferation into the intervertebral foramen in oblique views and (*c*) a lateral dural defect or obliteration of a root sleeve in the myelogram. I have seen 2 cases of combined rupture of cervical and lumbar vertebral disk in which classic defects were revealed in the myelogram.

Operative Approach: I strongly advocate the upright "cerebellar" position. A buttonhole unilateral approach, with laminotomy, similar to the lumbar approach, is used. The hole through the overlapping laminas can best be made with a high speed spherical drill, followed by chisel and curet. The dural root sleeve comes off at right angles to the dura, in contrast to the lumbar root sleeves. This prevents displacement of the dural sleeve during removal of the ruptured disk. The cervical intervertebral space is too narrow to permit insertion of pituitary rongeurs. The best that can be done is (*a*) to remove any "soft" fragments of a protruded nucleus (rare); (*b*) curet the interspace with a small curet (difficult); (*c*) remove with curet, nail punch or dental chisel, any cartilaginous ridge (beware of stimulating further proliferation of bone), and, lastly, (*d*) cut the sensory root (three fourths of the total diameter of the root) and occasionally transplant the motor portion of the root in a cephalad direction by slitting the dura upward. This was done in 5 cases, with improvement in motor (triceps) function and no appreciable sensory loss.

I wish to congratulate Dr. Michelsen on his excellent survey; I believe his operative series constitutes one of the largest in the United States.

MAJOR F. H. LEWEY, M. C., A. U. S.: Rupture of the intervertebral disk seems to occur as a result of infraction of the epiphysial plate of the upper and lower

adjacent vertebrae, subsequent slipping of the disk and eventual biting off of its protruded part by the sharp edges of the vertebrae in a sudden dorsiflexion of the spine. The possibility of an epiphysial infraction is facilitated by the persistence of a certain stage of normal embryonic development in many normal persons.

DR. SAMUEL LOWIS: A patient with rupture of a disk of recent traumatic origin at the fourth cervical interspace, with compression of the fifth cervical root, showed the following signs: diminution of the biceps reflex, pain extending into the anterior aspect of the forearm on the lateral side and into the medial side of the axilla; an area of diminished sensation on the anterior surface of the upper arm adjacent to the axilla and another area of diminished sensation at the base of the thumb, with no signs or other symptoms referable to the hand or fingers, and pain and tenderness in the interscapular and suprascapular areas.

DR. JOSEPH F. DORSEY: I should like to ask Dr. Michelsen whether one should obtain a myelogram in all cases of ruptured cervical disk. Roentgenograms of the cervical portion of the spine show narrowing at the affected interspace. In addition, the level may be localized precisely by neurologic examination. When a hemilaminectomy is done, two roots are usually visualized, so that the chance of an error in the level of the operative site is minimal. To me it would seem that myelography is an unnecessary procedure.

DR. JOST J. MICHELSEN: The average age of our patients was 45, the youngest being 32 and the oldest 68. Differential diagnosis of the scalenus anticus syndrome and root compression may be difficult indeed. However, the sensory manifestations of root compression have a different distribution. Only with lesions at the seventh interspace may they resemble those of neuritis of the lower part of the brachial plexus, of mechanical origin. The postural factors are different, too. Aggravation by certain movements of the neck, as well as by coughing and sneezing, is suggestive of an intraspinal lesion; certain movements which relieve the discomfort in cases of ruptured disk aggravate pain and paresthesias in cases of a spastic scalenus anticus muscle. Changes in the blood pressure and pulse, which are common with, and diagnostic of, compression of the brachial plexus, are absent with ruptured disk. Injection of procaine into the scalenus anticus muscle may be helpful. Myelographic studies in doubtful cases will usually determine the site of the lesion when other methods fail. As to the surgical procedure, Major Scoville has answered some of the questions. We have not had any difficulty in using the ordinary instruments for laminectomy, namely, the duck bill rongeur, the Kerrison rongeur and, occasionally, a small chisel and hammer. The ruptured disk was removed either extradurally or intradurally. In all the cases in which operation was performed free fragments of cartilage were lifted out with a forceps, without dissection or curettement. I have omitted another case in which there were exostoses, which Major Scoville mentioned. In 1 of our cases the posterior root was sectioned after removal of the fragment of disk. All the patients recovered after the operation; only 1 recurrence has so far been observed. Myelographic studies were performed for several reasons. It was felt that the presumptive diagnosis of this relatively new entity should be confirmed by unequivocal evidence of the type, location and size of the lesion. We have not had much success with the neck compression test. Perhaps we did not use it correctly. If the reaction was positive, simple tilting of the head toward the side of the lesion precipitated or aggravated the discomfort, too. The indication for operation was based on the degree of disability. In all cases some type of conservative treatment had been given before the patients were sent to us; in 2 cases exploration was not done, since the discomfort was not severe enough to warrant operation.

Effect of Anoxia as Measured with the Electroencephalogram and the Interaction Chronogram in Psychoneurotic Patients. DR. JACOB E. FINESINGER, DR. ERICH LINDEMANN, DR. MARY A. B. BRAZIER and DR. ELIOT D. CHAPPLE.

This paper will be published in full in the *American Journal of Psychiatry*.

Studies on the Physiology of Flight: Effect of Anoxia on the Electroencephalogram of Psychoneurotic and Normal Adults. Dr. Mary A. B. Brazier.

In the field of electroencephalography, the crux of the problem can be expressed in the form of two questions: (1) Where do the currents originate, and (2) What determines the frequency at which they oscillate? The answer to the first question is fairly well established, and it is generally recognized that the origin of the electrical potentials is in the cells of the cerebral cortex. The second question has not yet been fully answered, but a body of evidence is being collected to indicate that the rate of oscillation of these potentials is directly correlated with the rate of metabolism in the cells of the cerebral cortex. This evidence has accumulated from observations of the following type; if the metabolism of the cortex is upset by its being deprived of sufficient substrate, namely, glucose, the electroencephalogram will show slowing. If the metabolism of these cells is stimulated by some such agent as thyroxin or pyrexia, the electroencephalographic frequency again will speed up; or if the metabolism of these cells is depressed by depriving them of sufficient oxygen, the electroencephalogram, again, will reflect the change. The last situation, in which the electroencephalogram responds to anoxia, is the subject of this study.

Berger was the first to show that lowering of the oxygen concentration of the inspired air slowed the rate of the cortical potentials, and this observation has since been abundantly confirmed by other investigators. It was the purpose in this study to apply this fact as an objective method for assessing the degree of response of a subject to low oxygen concentrations, and this entailed the development of a method of measurement of these rhythms in order to be able to quantitate any change which took place.

A tracing was shown of a normal electroencephalogram, taken while the subject was breathing air. Below it was the record of the same subject when breathing a mixture containing only 8.8 per cent oxygen (a mixture simulating an altitude of 20,000 feet [6,060 meters]). The slowing of the electroencephalographic rhythm was obvious to the naked eye; but in order to measure the exact degree of slowing, a method had been developed for quantitative analysis of these records.

A measuring rule, originally designed by Dr. Hallowell Davis, was used for this work. It consists of a transparent sheet marked off for the various frequencies; this sheet is laid over the electroencephalographic record so that the interval between peaks of the waves can be determined and their frequency read off from the figures at the side of the scale. In this way it is possible to determine the percentage of each record which is covered by waves of the various frequencies, and a distribution curve can be assembled representing the amount of each frequency present. An example of such an analysis was shown.

In the sample shown, the greater portion of the record consisted of waves of 10 cycles per second, with lesser amounts of other frequencies, so that the distribution curve of the frequencies showed a peak at 10 cycles. If any slowing of this electroencephalographic rhythm took place, owing to the subject's breathing air of low oxygen content, one would expect the whole distribution curve to move to the left, into the range of slower frequencies, and this, in fact, was what was observed.

A tracing was shown, which was for 1 subject only, with a solid line representing the distribution of frequencies in the electroencephalogram when air was breathed, and a broken line the distribution when the oxygen was reduced to 8.1 per cent (equivalent to an altitude of 22,000 feet [6,666 meters]). At the low oxygen level, the whole curve had shifted to the left, into the slower frequency range. There were many features of this shift which might be used as measurements. For example, the amount of activity slower than a certain frequency could be used, and this would obviously be greater in the left hand curve than in the right and would give some measure of the slowing of the electroencephalographic

potentials; or one could use the shift of the peak of the curve, which is called the dominant frequency, since that was the frequency which dominated the whole of the electroencephalographic tracing. For the purposes of simplicity and brevity, the latter feature was presented only in the data which follow.

In this subject's record the dominant frequency shifted by ½ a cycle when the oxygen was reduced. In any large group of subjects who are breathing air the dominant frequency varies from person to person, but when charted it shows a distribution curve around the most common value for normal people, which is 10 to 10.5 cycles per second.

Such a distribution curve was shown for 37 subjects breathing air, together with the shift for the same 37 subjects to slower frequencies at oxygen levels below 11 per cent (i. e., at simulated altitudes above 15,000 feet [4,545 meters]). The degree of this shift was statistically significant. This chart showed a difference between the electroencephalograms of a group of subjects breathing air and those of subjects at low oxygen levels, but it did not give information as to whether this slowing takes place suddenly at an altitude of, perhaps, 15,000 feet or whether it is a response which is correlated with the level of anoxia involved.

In a table, the same series of 37 subjects were divided into three portions: those at oxygen levels below 9 per cent (i. e., above 20,000 feet); those at oxygen levels between 9 and 10 per cent (18,000 to 20,000 feet [5,454 to 6,060 meters]), and those at oxygen levels between 10 and 11 per cent (15,000 to 18,000 feet). It is immediately clear that the average slowing was greater the lower the oxygen level. Here, then, is one variable which affects the degree of slowing; in other words, the degree of slowing is dependent on the degree of anoxia. There is, however, another variable at work, the carbon dioxide level. Great technical difficulty was experienced in eliminating all the expired carbon dioxide from the circuit, since it accumulated so quickly and some inevitably remained to be rebreathed. In none of the 37 cases reported here was the inspired carbon dioxide over 0.5 per cent, but a striking difference was found in the degree of response to low oxygen levels between those subjects who were breathing less than 0.3 per cent carbon dioxide and those who were breathing between 0.3 and 0.5 per cent carbon dioxide. There was a greater slowing of the electroencephalogram at the lower carbon dioxide levels.

When both the oxygen and the carbon dioxide level were low, there was the greatest slowing of the electroencephalogram. When the oxygen was reduced only to the 10 to 11 per cent level and the carbon dioxide was over 0.3 per cent, the electroencephalogram showed no slowing. The influence of carbon dioxide on the reaction of subjects in low oxygen concentrations was expected from all the work that has been done in this field, but it was an unexpected result to find that carbon dioxide exerted its influence in such low concentrations as 0.3 per cent.

These two variables, the oxygen and the carbon dioxide level, were, however, not the only two variables in the present data. In the original group of subjects under discussion, there was a third variable; namely, that of this population 25 were psychoneurotic patients and 12 were normal adults. Since it was one of the objectives of this study to determine whether patients with psychoneuroses reacted to oxygen deprivation in the same way as normal subjects, the results have been analyzed from this point of view.

To simplify the issue, one variable was eliminated from this analysis, namely, the influence of carbon dioxide. Only those experiments in which the carbon dioxide was less than 0.3 per cent were included; hence, only 18 subjects were included. It was found that the electroencephalograms of the psychoneurotic patients showed a greater degree of slowing than did those of the normal adults. The difference found by measurement was of statistical significance. This finding that the psychoneurotic patients show a greater slowing of their electroencephalo-

graphic frequencies under anoxic conditions than do normal adults has many implications, especially if one goes back to the opening question raised in this paper; namely, that the frequency of electroencephalographic potentials reflects directly the condition of metabolism in the cortical cells. The electroencephalographic results suggest that the metabolism of the cortical cells of the psychoneurotic patients is more labile than that of normal adults.

DISCUSSION ON PAPERS BY DR. FINESINGER AND ASSOCIATES AND DR. BRAZIER

MAJOR F. H. LEWEY, M. C., A. U. S.: This is a series of stimulating and interesting experiments and observations. I was specifically impressed by Dr. Brazier's contribution, realizing how much more information can be derived from the electroencephalogram by application of statistical methods.

Did I understand Dr. Finesinger correctly as stating that the changes of frequency of the electroencephalogram under his experimental conditions followed Arrhenius' equation? This would mean that the reaction time of the physicochemical processes underlying the electrical potentials of the electroencephalogram rises with the temperature but that the irregularity of this so-called coefficient of temperature followed Arrhenius' rather than van't Hoff's, equation. Was this statement meant to be an analogy, or did the group of patients with increased or decreased activity show changes in their temperature characteristics?

DR. WILLIAM G. LENNOX: I want to express my appreciation of this well integrated and well coordinated study. I hesitate to suggest additions to the already complicated observations, but I wish Dr. Finesinger had made use of his technic for recording the pulmonary ventilation. Lack of oxygen induces increased respiration, which, in turn, sharply alters the carbon dioxide content of alveolar air and of arterial and cerebral capillary blood. Therefore I object to the title, which implies that observed changes in the electroencephalogram are due to anoxemia alone. Measurement of the small variations in the carbon dioxide content of inspired air can be of no significance, for the severe anoxemia induces hyperpnea, which greatly decreases the carbon dioxide content of arterial blood. The relative importance of oxygen and of carbon dioxide in altering the frequency of brain waves can be decided only by measuring the levels of these two gases in the blood entering and leaving the brain. Dr. and Mrs. Gibbs and I made observations of this sort after putting a needle into an internal jugular vein and another in a femoral artery. We found that carbon dioxide was more influential in altering brain wave frequencies than was oxygen. We could carry subjects to unconsciousness with anoxemia; but if we kept constant the levels of carbon dioxide in the arterial blood there was no appreciable slowing of brain waves. Dr. Brazier suggested that unusual effects in neurotic patients may be due to something specific in the metabolism of the neurons of these patients. Possibly, however, such persons have an unusual respiratory response to anoxemia, which would cause unusual changes in the carbon dioxide content and in the brain waves. Again, their cerebral circulation might respond in an unusual way to a given change in the oxygen or the carbon dioxide level of the arterial blood. We observed that patients with petit mal had unusual slowing of brain waves with hyperpnea. We found that this slowing was due to failure of the cerebral arterioles to constrict with overventilation. Failure of constriction meant failure of slowing of the blood flow, and hence lowering of carbon dioxide tension in the capillaries and resultant slowing of the brain waves. Some such mechanism in neurotic patients would seem simpler than postulation of a cortical cell metabolism which is specific for neurotic persons.

LIEUT. COL. JACKSON M. THOMAS, M. C., A. U. S.: I am not qualified to comment on the oxygen and carbon dioxide factors studied in this investigation. As a clinical psychiatrist, however, I should like to know what sort of questions the patients were asked. What was the nature of the interviews? I wonder whether all the patients should be classified as psychoneurotic. The speaker's use of the words "activity" and "inactivity" in describing the patients puzzles me.

DR. ERICH LINDEMANN: In order to obtain a comparison of the clinical behavior of subjects during the experimental interviews, we obtained disk recordings of the verbal interaction between the patient and the interviewer. The changes in behavior noticeable were of two types. In one type the patients became restless, appeared distressed and demanded permission to leave the anoxia chamber—this was likely to happen during the mixing period. In the other type, the patient became increasingly uncommunicative and then ceased to respond altogether, so that the experiment had to be interrupted. These two extremes, acute apprehension with restlessness, on the one side, and apathy with failure to respond, on the other, seemed to be two poles of a continuous series presenting various combinations of the factors mentioned. It is of interest that the restless state was often attended by phenomena suggesting autonomic stimulation—sighing respiration, flushed face and profuse sweating—while the apathetic state seemed to progress insidiously without any such dramatic manifestations.

During the second interview, as the experiment proceeded, we again noticed two different states: one of overactivity, with somewhat garrulous talking with euphoria; the other of reduced communication, shorter responses, stereotyped answers and inaccurate answers. In addition, we noticed evidence of the disintegration of language; there were no complicated sentences and frequently only fragments of sentences, monosyllabic answers. There was also some dysarthria.

The complexities of the changes in the clinical behavior suggested that they involved not only the effect of anoxia on cortical functions but also effects on the autonomic nervous system, probably related to stimulation of the carotid sinus. In former work, Dr. Finesinger and I were able to show that injections of epinephrine and mecholyl may be followed by pronounced changes in the rate of verbal activity of psychiatric patients during interviews, the former reducing and the latter increasing activity. It is likely that the changes in the rate and quality of verbal activity result from both factors, autonomic and cortical.

That autonomic stimulation may occur at smaller degrees of reduction in oxygen than interfere in cortical functions would explain why changes in rate of activity were observed at relatively high levels of oxygen, while changes in the electroencephalogram appeared only at more pronounced degrees of anoxia.

DR. JACOB E. FINESINGER: In reply to Colonel Thomas' question: The basis of our diagnosis was description of symptoms. The patient has disorders diagnosed as anxiety neurosis, hysteria, reactive depressions and combat neurosis—the kind of patient seen here today. We tried to control the topics in the interview. We tried to keep away from charged topics. We thought the school topic was probably not a charged topic for most people. We tried to standardize the interview as best we could, knowing that there were gaps. As to activity and inactivity, Dr. Chapple will comment on that.

DR. ELIOT D. CHAPPLE: We mentioned the work of Stier and Pincus on respiration and activity in order to point out that some of the mechanisms of control activity were possibly located in the lower centers, not to imply that we were changing the temperature of our subjects in order to use the Arrhenius equation.

DR. MARY A. B. BRAZIER: In reply to Dr. Lennox: It would add considerably to knowledge of the effect of anoxia on cerebral activity to have information from the blood stream, but in this particular experimental situation, in which we try to have as normal an interview as possible, such manipulation is out of the question. I agree that the data presented here are not critical in deciding the roles of oxygen and carbon dioxide, but such critical data do exist and have come from another laboratory. Since the originator of that work is here tonight, I shall ask him to answer that question.

DR. HUDSON HOAGLAND, Worcester, Mass.: The fact that brain wave frequencies may correlate better with the content of blood coming from the brain than they do with the corresponding oxygen content does not at all militate against the view of the importance of cell respiration as a determinant of brain wave frequencies.

There is a large factor of safety for oxygen transported to the brain, and hence oxygen tension can be considerably reduced without modifying cerebral respiration, since the limiting factor is the degree of saturation of enzymes and this is not affected until after considerable reduction in the oxygen content of the blood.

It seems to me that there is one set of experiments which conclusively demonstrates that alpha frequencies are directly proportional to cerebral respiration. These experiments have been published in a series of papers by our group at Clark University since 1936 and were reviewed in 1944 (Hoagland, H.: Colloid Chemistry, edited by J. Alexander, New York, Reinhold Publishing Corporation, 1944, vol. 5). They show that the "energies of activation" of the processes determining alpha frequencies are identical with those found for certain specific key respiratory enzymes studied in vitro and known to be limiting factors in cerebral respiration. There is no way in which the results of these experiments can be interpreted except in terms of this view, namely, that the frequencies in resting subjects, with closed eyes, are directly proportional to the speed of certain chemical steps (specific enzyme pacemakers, or bottlenecks) in the sequence of cellular respiration. This view is consistent with our findings that dinitrophenol and thyroxin speed the rhythms and with our observations and those of other investigators showing that alpha frequencies are slowed by hypoglycemia.

According to my view, carbon dioxide as an acid metabolite produced by cellular respiration is an important agent in firing the cell. Its production in the cell is a direct determinant in the cell's recovery from its refractory phase, since it acts to determine potassium diffusion gradients, which are the basis of bioelectric potentials according to work from a number of laboratories. Thus the more carbon dioxide is produced the more rapid the recovery, and hence the faster the frequency of firing of the cells. This view is not inconsistent with what is known of the role of acetylcholine in relation to bioelectric potentials. Of course, the absolute frequency of firing of a chain of cells depends on the electrical constants of the tissues, as well as on respiration; but these electrical constants must average as stable values for any given group of cells, such as those contributing to the alpha rhythm in the resting subject with closed eyes. Otherwise, the results obtained in our measurements of energies of activation, previously referred to, relating alpha frequency to respiratory enzyme systems, would not have been obtainable.

There is, thus, no meaning to the controversy about oxygen versus carbon dioxide in relation to the dynamics of brain waves. Carbon dioxide produced at a rate proportional to the cell's respiration (respiratory quotient of the brain is unity) can fire the cell by creating potassium potentials. If this mechanism is correct, one should expect the results obtained by Gibbs and others, who have found that brain wave frequencies parallel more closely the carbon dioxide than the oxygen content of the blood when air containing varying amounts of carbon dioxide and oxygen is breathed.

Madelaine R. Brown, M.D., *Presiding*

Regular Meeting, Oct. 18, 1945

A New Psychiatric Rating Scale. Dr. William Malamud and Dr. Hudson Hoagland, Worcester, Mass., and Lieutenant I. Charles Kaufman, Medical Corps, Army of the United States.

Quantitative rating of the degrees of intensity in the course of mental illness is of fundamental importance if changes in the behavior of patients with mental disease are to be correlated with physiologic and biochemical data.

Twenty items of significance in the evaluation of the status of psychotic patients were selected. These items were chosen on the basis of two factors:

(*a*) items in which the degree of variation from the average or normal was meaningful; (*b*) items which could be observed and evaluated equally well by independent observers. The functions selected fell into three groups: (1) those that could be observed directly during an interview, (2) those that could be obtained through communication with the patient during an interview and (3) those aspects of behavior that could be observed by the ward personnel over a twenty-four hour period.

Numerical values were assigned to each of these items, describing their degree of departure from normal in a given case. The maximum departure for each function from the zero norm was 2 units, and thus the rating of an individual patient might range from zero to 40 units.

Three psychiatrists independently rated each of 20 schizophrenic patients interviewed by one psychiatrist in the presence of the other two, and each physician independently recorded his score. Correlation coefficients were then determined to test the scale. The scores of Dr. M. correlated with those of Dr. F., giving an r value of 0.907 ($P < 0.01$), and Dr. M.'s scores correlated with those of Dr. K., giving an r value of 0.868 ($P < 0.01$). It was found that instructed nurses can use the scale so as to give meaningful ratings of psychiatric status when compared with ratings given independently by a psychiatrist. The data indicate that the criteria underlying the ratings are sufficiently communicable and reproducible to make the scale practically serviceable in quantitating the over-all degree of the psychotic state.

DISCUSSION

DR. FREDERICK L. WELLS: It is obvious that these presentations open an enormous field of discussion. It is only from one point of view that it would be pertinent for me to speak; that is with regard to Dr. Malamud's rating scale. When one has been in this field for a number of years, one becomes imbued with the historical point of view. I never like to miss saying a word for my old teacher, Dr. James McKeen Cattell, who really started this sort of thing; he had the whole rating scale idea developed in the early 1900's. Then, curiously, it dropped out of sight. Twenty years later it reappeared. Textbooks make little reference to Cattell in the matter. The multidimensional approach has been made explicit under the name of *Gestalt*. Since the days of early Greek philosophers, it has been known that the whole is greater than the sum of its parts. When the scale was put on the screen, I thought that we were going to see how these specific traits show up and how people agree with respect, for example, to memory or sex responses; what we actually have is a presentation based on the summated score of all these traits. A group of clinical psychologists would want to know the agreement with regard to the specific traits of the scale, and they would question whether these various traits arrange themselves in a linear scale quite as effectively as they should for a rating on specific traits. One is faced with the question, "How much does this scale add to what would be learned if the psychiatrist asked, 'How well is this patient?'" Is not the result the same except that the conclusion is arrived at by a summation of traits rather than by a single one? Such rating scales have been used at Worcester before. I recall some rather elaborate procedures of the sort in Dr. Hoskins' research on dementia precox. To come back to the statistical point of view, it is interesting to compare this scale with other attempts of the same kind. When Dr. James S. Plant and I were at McLean Hospital, we discussed the possibility of constructing such a scale, and he published the method in the *American Journal of Psychiatry* in 1922.

With regard to global traits, these traits have to be broken down. Take memory, for example. Memory is a function made up of many components. I wonder how justified one is in lumping a number of traits like these. Wechsler has brought out a memory scale. He has pointed out that I was the first person to use the term "memory quotient"; I fear it would be better for psychologic discipline if I had also been the last.

Dr. Malamud's point is well taken—that one cannot get a satisfactory picture of a patient, and certainly not of a normal person, with rating scales, but that one has to have rating scales for purposes of comparison. Psychologists use them too much in evaluation of personality when they have no contact with the actual person; they are simply numbers attached to trait names. Statistically, it seems valid, but as soon as one has to square the rating scale with a fair psychiatric evaluation of personality, there is trouble. A rating of this type cannot tell anything like the whole truth about the patient. Ultimately one needs another sort of multidimensional approach—from various levels. One can well start with the fundamental concepts of Edward J. Kempf and work through Sheldon's ideas on "temperament," though with no commitments on the somatic side. A next step is through the penetrating scheme of personality traits developed by Henry A. Murray.

I should like to ask one question with respect to the history of these patients: Has there been any observation of their prepsychotic personalities?

Dr. Frederick Wyatt: Dr. Malamud, in his interesting report, has touched on some of the difficulties of his experiment. In his attempt to rate behavior, his predicament is familiar to the psychologist. We psychologists are constantly under pressure to achieve standards of quantitative exactness in our work such as the natural scientists keep dangling before our eyes. We have certainly tried hard. I wonder, however, whether in psychologic and psychiatric work we are not dealing with a material which *a priori* does not lend itself to the methods of some of the natural sciences. It has yet to be shown that the standards and methods specific for them are necessarily binding for all scientific endeavors.

Three problems have always been encountered with rating scales: 1. Which traits or modes of behavior should be selected as the important ones? 2. How can these observations be transformed into quantities? 3. What will the measure of quantification be, or what set of data will supply the standards against which the individual case is held and rated as high or low? With regard to the first two questions, I could grasp only a few of the variables shown on the slide. In one of them, homosexual and masturbatory behavior seemed to be to the right of the middle line, while sexual behavior and exhibitionism were to the left. So far as present knowledge goes, each of these forms of sexual behavior is quite complex in itself, as is their dynamic basis. On the quantitative basis proposed, twice the rating for homosexuality would equal the rating for exhibitionism. I am quite aware that Dr. Malamud and his associates had nothing of this kind in mind. Yet the reduction to absurdity may show the difficulties inherent in the transmutation of complex behavior patterns into additive quantities.

Now to the third point: What standards should the rating follow? The problem has two sides. One is the consistency of the observer in his own rating; the other is the position of the subject with regard to the features of the rating scale and involves the question of the uniformity of the population. In our work, my colleagues and I deal with a great variety of people. What does "premorbid personality" mean in the sense used here? Prior to his psychotic breakdown, a patient may have had marked homosexual tendencies; yet they may not have interfered with his general adjustment. The consistency of the rating observer seems to me to offer the gravest problem. How can he know whether he should rate the first members of his population high or low when only a larger group will indicate representative trends and changes. His idea of an average value for any of the qualities in the group shifts with the number of people whom he is seeing—often unnoticeably so. Under these conditions, he can never be quite certain whether he is consistent in his rating from one member of the population to the next. Furthermore, the psychiatrist is likely to rate a patient differently in the light of what he has learned about him during several months of observation.

Of the desirability of a rating scale such as the one presented here there is no question. A more extensive scale was published some time ago in the

Journal of Abnormal and Social Psychology. Dr. Malamud's scale has the advantage of being more concise. I should like to mention the rating of personality traits and behavior in a recent study at the Harvard Psychological Clinic in which I participated. First, the traits of each subject were rated by a group of observers individually and were unified only after contradictions in rating had been discussed and clarified.

DR. ROY G. HOSKINS: The question of other rating scales has been raised. Our previous experiences at Worcester have been numerous and have entailed the many perplexities that the discussers know are there. Twelve or fifteen years ago, my colleagues and I studied the Kempf scales, as used at the Phipps Clinic; the Plant scale, and various others. Then we selected about one hundred and forty traits and had four psychiatrists apply the rating scale for those traits to a group of patients. As standards we selected patients who were fairly representative and in a stable condition. Some of the traits failed to correlate with anything significant. The number of traits was ultimately reduced to about forty, which correlated rather well. At that point we realized that we must either have more psychiatrists or work only on rating scales; we decided, therefore, to go on with other activities and left the matter in abeyance. The crux of any of these systems is the weighting, as Dr. Wells suggested. It is possible that ten traits properly selected and weighted would be quite as adequate as any larger number. Dr. Wells asked how our simple over-all five point rating system worked. It proved to be fairly satisfactory. Perhaps the chief advantage of a composite scale is the confidence that is afforded the psychiatrist in his over-all judgment. One's thoughts go to Mephistopheles and the student: "How comforting it is to have so many things in one's notebook." Actually, the combined judgment of the psychiatrists as to the degree of severity of the psychosis at any given time correlated about as well as in any other system we have used. Dr. Malamud informs me that the traits selected for his new scale are actually those which he has long used in making clinical appraisals of the psychosis in connection with which it was employed. The result, no doubt, is a schema that would function adequately in a service managed by Dr. Malamud. Some other man in some other service might do better with a scale of his own devising.

DR. WILLIAM MALAMUD: I am grateful to the discussants for their interest in this method of approach and their helpful criticisms. Dr. Wells and Dr. Wyatt discussed the rating scale along rather similar lines. Dr. Wells reminded us of previous attempts to construct rating scales; I wish to assure him that we were aware of these and have taken them into consideration. The only reason we speak of the present scale as "new" is that it is specially applicable in correlating psychiatric findings with special types of physiologic data.

Dr. Wyatt asked whether the rating scale was devised as an attempt to compensate for a feeling of inferiority in relation to the exact sciences. Certainly not! It was, I should say, an attempt to adjust ourselves to a group with whom we were working but who expressed themselves in a manner different from ours. In our clinical work and in our evaluation of the condition of our patients from day to day, we have always made use of some form of quantitative measure. Otherwise, we could not speak of relative degrees of seriousness of the patients' maladjustments. The present scale is simply a translation of this method of evaluation into terms which lend themselves to correlation with physiologic data.

The question was asked as to our standards of comparison. So far as possible, we try to use as a base line the behavior of the patient prior to his disease. Obviously, we have to rely mostly on the history as obtained from the relatives. Here, again, we have followed established clinical procedure. When a patient's condition is evaluated, we ask ourselves: In what way is his present behavior different from that which people usually expected of him? The "usually expected" is what we take as the average, or C, level, and the deviations are judged in relation to this norm.

Dr. Wyatt wishes to know whether the psychiatrist's ability to use the scale does not improve with experience. Obviously it does. This is true of the use of any method of evaluation. However, the difference is not quite so great as might appear likely. Thus comparison of the results of my rating and those of Dr. Kaufman's showed little discrepancy, whereas there is considerable difference in the number of years the two of us have worked in this field. The important factor is that the items rated are in the main objective and are therefore not particularly dependent on personal impression. If a person is mute or refuses to eat or is untidy about his personal appearance, there really is not much room for differences in recording such a fact. Similarly, if the patient states that he is sad or angry, it does not matter how experienced the person is who records such a statement. The scale, however, is particularly useful for the day by day rating of a patient by the same physician. Under such conditions, the differences can indicate only changes in the patient's condition.

Dr. Wells's question concerning the prepsychotic personality of persons with involutional psychosis will perhaps take us too far afield. I refer him to the work of H. D. Palmer and to our own previous publication (Malamud, W.; Sands, S. L., and Malamud, I.: *Psychosom.Med.* **3**:410, [Oct.] 1941).

Changes in the Electroencephalogram and in the Excretion of 17-Keto Steroids Accompanying Electroshock Therapy of Agitated Depression. Dr. Hudson Hoagland and Dr. William Malamud, Worcester, Mass.; Lieutenant I. Charles Kaufman, Medical Corps, Army of the United States, and Dr. Gregory Pincus, Worcester, Mass.

The psychiatric rating scale discussed in the preceding article was used in the study of 13 women with agitated depression. Ratings were made not less than three times a week—before, during and after periods of eight to fifteen electroshock treatments. Electroencephalograms were recorded over these same periods twice a week. During the treatment period (two shocks per week) the electroencephalograms were taken on the day following that of shock treatment. Samples of urine were also collected from time to time during the pretreatment, treatment and post-treatment periods.

The psychiatric ratings were found to correlate well with fast (greater than 13 per second) frequencies in the electroencephalograms. When the patient improved, the percentage of time these waves were present was reduced. However, there was also a tendency for the fast waves to return in some patients showing good remission.

The diurnal rhythm of the morning rate of 17-keto steroid excretion divided by the night rate was calculated as a measure of adrenal cortical activity. While in normal persons this value is 1.60, in the patients studied the mean pretreatment value was 1.03; during treatment the mean value rose to 1.32 and in the post-treatment period it declined to 1.25.

The possible significance of these findings was discussed in terms of questions they raise for future exploration.

DISCUSSION

Dr. Robert Schwab: In a recent paper (*Am. J. Psychiat.* **102**:49 [July] 1945) Bagchi, Howell and Schindle described the electroencephalogram before and after electric shock. They pointed out that it was a long time before the electroencephalogram returned to normal after shock treatments. The delay was related to the number and severity of the shock treatments. I agree that it is important to correlate certain changes in a particular part of the brain wave spectrum with clinical findings before and after shock therapy, but it is equally important to keep an eye on the total brain wave picture. I should like to ask Dr. Hoagland how much time elapsed after the shock before the electroencephalographic records were obtained. It is well known that after electric shock convulsions or, indeed, after ordinary convulsions, the equilibrium of the electroencephalogram is disturbed for several days. I feel uneasy in

attaching much importance to small changes, particularly the faster frequencies, found during that period of cerebral electric instability.

It has long been a temptation to physicians, particularly to psychiatrists, to have a rating scale of clinical symptoms and disabilities on a numerical basis comparable in simplicity to those used by ophthalmologists in rating visual acuity. I utilized such a scale in my psychiatric work overseas during the past two years, but most of my psychiatric colleagues were rather contemptuous of anything so simple. It is important, in my estimation, that efforts of this sort be extended and encouraged, as something may ultimately be worked out that will satisfy psychiatrists, laboratory workers and general practitioners.

Dr. Rudolph Neustadt: In 1941 my colleagues and I studied a group of 11 patients before and after electric shock therapy with respect to changes in their blood chemistry. There were no changes in the hemoglobin content or in the white or the red cell count. Changes in cholesterol were inconclusive, as some patients showed an increase and others a decrease after treatment. In some patients the blood sugar increased after each shock treatment but returned to normal within a day. In all patients the blood creatinine showed a slight increase after each shock but returned to normal within twenty-four hours. All patients showed a decrease in the 17-keto steroid excretion of 50 to 70 per cent from the pretreatment level, and it required eight to ten weeks for the output to return to the previous level. There also was a striking reduction of creatinine in the urine. These findings indicate that electric shock treatment puts a great stress on the endocrine system, particularly the adrenal cortex. It takes a long time to recover from the effects of electric shock treatment. I cannot see how these figures compare with Dr. Hoagland's; however, it is possible that the balance between day and night excretion of ketosteroids is already restored at a time when the excretion of total ketosteroids is still lowered.

Dr. Hudson Hoagland, Worcester, Mass.: I mentioned that our results, together with other, earlier evidence in the literature, indicated dramatic changes in the electroencephalogram following electroshock treatment in some patients. These changes usually take some time to subside when the series of treatments is over. They consist of slowing and increased amplitude of frequences of less than 12 per second. But these effects do not correlate with directional changes in the psychiatric state. As I said, our records were always taken on days between shocks and were always spaced so as to occur either one day, for certain patients, or two days, for others, after shock. Two shocks were given and two electroencephalograms were obtained per patient each week, and the changes in the components of more than 13 cycles per second usually showed pronounced differences in a given patient between times when she was ill and times when she was well. Each patient was thus her own control. Twenty-five fold variations, from 50 to 2 per cent, in the amount of time the fast frequencies were present were not unusual, and these were very real changes. Because the amplitudes in this frequency range are low and the waves are irregular, the changes were not especially striking on casual inspection of the record. In instances of psychiatric relapse during the course of shock treatments, our figures indicate that these frequencies again come to occupy an increasing percentage of the record, and this fact militates against the view that they are products of the treatment per se, since the treatment is continuing routinely. The point is that our figures show a parallelism of the frequencies greater than 13 cycles per second with the psychiatric state.

I should like to ask Dr. Pincus to answer Dr. Neustadt's question.

Dr. Gregory Pincus, Worcester, Mass.: Our data are not very decisive. Before shock treatment there appears to be great variability in the absolute levels

of 17-keto steroids excreted. In a number of women we found much higher levels than one would expect for persons of that age and sex. The output varied a great deal. The only thing that showed consistency was the sleep:waking ratio, which was 1 or slightly above or slightly below. In some patients the absolute level fell after shock treatment. That is about all I can say on that point, and I think that the explanation offered may not be the only one. It does not necessarily follow that the shock treatment has lowered the output level. At certain ages one might expect a lower level anyway.

Relation of Changes in Carbohydrate Metabolism and Psychotic States.

DR. HARRY FREEMAN and DR. RALPH N. ZABARENKO, Worcester, Mass.

A study was made of the relation of the dextrose tolerance and the psychiatric state in 28 acutely psychotic patients who were receiving electric shock therapy. The patients included 11 men and 17 women. Their average age was 30. Sixteen of the subjects had schizophrenia, while the disturbances of the others had been diagnosed as involutional melancholia, bromide intoxication, psychoneurosis and manic-depressive psychosis. Dextrose tolerance tests (Exton-Rose technic) were made before shock therapy was instituted and at monthly periods thereafter for an average of six months.

Before treatment was begun, the dextrose tolerance of almost all the patients was grossly abnormal. There was a diabetic-like trend, indicative of a reduction in the ability to utilize dextrose. After treatment was finished, there were pronounced psychiatric improvement in 9 patients, moderate improvement in 12 patients, and no change in the other 7 patients. The dextrose tolerance obtained on the last occasion that the patient was seen was compared with values obtained before therapy was instituted. The patients were divided into three groups, depending on the degree of improvement, and mean values were obtained for each group before and after treatment. The data showed a tendency to lessening of the abnormality in the dextrose tolerance as a result of treatment in the group showing pronounced improvement, but the change was not significant.

Analysis of the individual cases showed a fairly good relation between the psychiatric observations and the type of dextrose tolerance obtained and indicated the reason for the lack of significance of the change in the mean values. In some patients a good social adjustment was made after treatment, and the dextrose tolerance became normal. In others the psychotic behavior disappeared but residual symptoms of anxiety and guilt feelings remained, and in such patients the dextrose tolerance remained abnormal.

It was the feeling of the authors that the abnormality in the dextrose tolerance depends primarily on the amount of emotional tension present in the patient, not on the psychopathic character of the behavior. It follows, therefore, that the sugar tolerance would become normal only when patients had sufficient insight into their problems so that they could deal with them in adequate fashion.

DISCUSSION

DR. ROY G. HOSKINS: Dr. Freeman has treated with a light touch a situation which my associates and I have faced for several years. We have been interested in the blood sugar in schizophrenia for a long time. Our interest was intensified when the war started and we worked with military patients, of whom we have had about 200. For about 70 per cent of these patients who came into the hospital with mental disturbances an apparently "diabetic" sugar curve was obtained, while comparable values were found in only about 30 per cent of normal control cases. Dr. Freeman has made many attempts to find out what the aberration means, what it correlates with. As he suggested, the correlation with anxiety is the most promising explanation, irrespective of the diagnosis the patient carries. That, however, is an unsatisfactory point at

which to leave the matter. One cannot explain a physiologic phenomenon by attaching a label to it. What is there about anxiety that leads to this aberration in the sugar curve? There are several possibilities. One is an interference with the normal insulin reaction. The level of adrenal cortical secretions might also be important. The thought that has been engaging my mind most recently is this: In a normal person the first provocative dose mobilizes the forces that handle sugar so that the second dose can promptly be dealt with and the sugar curve go no higher. It would seem that in schizophrenia the mechanism that normally takes care of the sugar is sluggish. Later it comes into function. A study of the reasons for this lag in the adaptation to hyperglycemia seems to offer the most promising point of attack.

DR. HARRY C. SOLOMON: Are these curves for acute psychotic subjects, and are the curves similar after several years of hospitalization?

DR. J. FOLCH: It is recognized that the central nervous system does not need insulin to handle sugar. In this test the central nervous system is acting on the system, not vice versa. It seems to me that the importance of this test would lie precisely in its being able to detect schizophrenia which would not be diagnosed by standard psychiatric examinations.

DR. RUDOLPH NEUSTADT: Spelberg and Leff examined some 30,000 inductees for glycosuria and found only 19 cases, but in 10 of these 19 cases an abnormal result in the Exton-Rose test was followed the next day by a normal sugar tolerance curve with the standard three hour test. This raises the question whether the Exton-Rose test, as applied by Dr. Freeman, is reliable enough for investigative purposes.

Dr. Freeman is right in being conservative in his conclusions. There was a correlation between the sugar tolerance and the mental status in the depressed patients, but there was no correlation in his schizophrenic patients. Some of the latter showed normal sugar tolerance curves before treatment and abnormal curves after treatment in spite of clinical improvement. These findings seem to me to be characteristic of schizophrenia. My colleagues and I have studied the carbohydrate metabolism (sugar, pyruvic acid and lactic acid in arterial and venous blood) for several years. We have found changes from normal to abnormal and vice versa from one day to the next without any obvious physical or mental changes in the condition of the patients. The only definite finding is that schizophrenic patients are entirely unreliable. This is in marked contrast to patients with manic-depressive psychosis.

Did those patients who had an abnormal sugar tolerance before treatment show any clinical symptoms of endocrine abnormalities?

DR. CLEMENS BENDA, Wrentham, Mass.: I am surprised that Dr. Freeman found only an increased sugar tolerance in his patients. I should like, therefore, to ask several questions. Several years ago Dr. Bixby and I published a paper on sugar tolerance tests in which we included observations on the Exton-Rose dextrose tolerance of patients with mongolism. We tried to adjust the doses of sugar according to the weight of the patient; I wonder whether Dr. Freeman did the same or used one standard dose for all patients. I wonder, also, whether any insulin tolerance tests were made on the same patients. Increased sugar tolerance is especially frequent with conditions associated with hypothyroidism. Were any cholesterol determinations or metabolism tests made on the same patients which would suggest hypothyroidism? Patients with anxiety are usually restless and overactive. Did Dr. Freeman find any instance of decreased sugar tolerance?

DR. ROBERT SCHWAB: In our work with chronic seasickness at the Naval Hospital here, three years ago, my colleagues and I found that subjects who were made sick on our "swing" had during this period an altered sugar tolerance curve so that the blood sugar hardly rose above normal. With the use of barium sulfate mixed with a dextrose meal, we proved that this was due to gastric stasis, the sugar mixture remaining in the stomach, blocked by the spasm of the pylorus produced by the motion sickness syndrome.

I wonder whether the reverse could occur in Dr. Freeman's patients. Could the dextrose leave the stomach more rapidly than it would in normal subjects and hence give a diabetic appearance to the curve? Did Dr. Freeman use barium sulfate with his dextrose mixture to ascertain whether this was so?

DR. HARRY FREEMAN, Worcester, Mass.: These dextrose tolerance curves were studied on acutely psychotic patients in the main. We have studied various types of patients, both psychotic and nonpsychotic, and have found that 70 per cent show abnormal trends, irrespective of the diagnostic subtype. It is our impression that the tolerance becomes increasingly abnormal as the emotional disturbance in the patient becomes more severe.

The accuracy of the Exton-Rose procedure in the diagnosis of diabetes is as high as that of the standard single dose procedure. The consistency of the two types of test is equally good, according to our own studies on nondiabetic subjects.

There is little value in adjusting the dose of dextrose to the weight of the subject. Studies in the literature show that after a minimum dose of dextrose is ingested, about 50 Gm., further increases have no effect on the height of the curve, although they do tend to prolong the duration of the hyperglycemia.

Insulin tolerance tests were made on about 90 patients. On the whole, the patients, irrespective of diagnostic subtypes, tended to show some resistance to insulin; 45 per cent of them showed a lesser fall in blood sugar than does any normal subject. However, there was no statistically significant relationship between the dextrose and the insulin tolerance of any given subject.

The thyroid gland does not play much of a role in the production of these abnormally high curves. Of the thyroid disorders, only hyperthyroidism produces a low tolerance similar to that found in these patients. However, our patients tended on the whole to have low basal metabolic rates, which one would expect to result in flat tolerance curves.

The problem of the absorption of the dextrose from the gastrointestinal tract is an important one. It would be expected that such high blood sugar values as we have found would result from excessively rapid rates of absorption. Studies on schizophrenic patients show that the rate of progress of a barium sulfate meal through the gastrointestinal tract is either normal or delayed. Furthermore, as another method of testing rates of absorption, we studied the absorption of xylose, a nonutilizable sugar, in patients with normal and with abnormal dextrose tolerance. There was no difference between the two groups; so it does not seem that varying rates of absorption account for the abnormalities in the dextrose tolerance values.

CHICAGO NEUROLOGICAL SOCIETY

Ben W. Lichtenstein, M.D., *President, in the Chair*

Regular Meeting, Jan. 8, 1946

Neuropsychiatry in the Mediterranean Theater of War. DR. BENJAMIN BOSHES.

Compound Spinal Injuries: Report of Two Cases. DR. MILTON TINSLEY.

Twenty-two cases of compound spinal wounds were analyzed, in 19 of which complete paralysis immediately followed injury. In all these cases early laminectomy was done. In 2 cases there was remarkable return of function, and these cases were reported in detail. In this series there was only 1 death and no postoperative infection.

Roentgenographic examination was found to be misleading; anatomically the degree of damage was far more extensive than the roentgenograms indicated. Indriven fragments of bone could not be visualized. The only possible way to do an adequate débridement was by formal laminectomy.

The presence of foreign bodies or indriven bone in the spinal cord sets up a series of pathologic changes, these lesions being similar to those produced by the presence of foreign material in the brain. It was felt that the removal of irritant foreign material prevented the development of cicatrization and further damage to the spinal cord. In addition, laminectomy allowed for repair of the dural defect and the reestablishment of normal circulation in and about the cord.

The following ideas were presented:

1. Laminectomy performed by a competent surgeon did not increase either the mortality or the morbidity.

2. The long after-care could be more intelligently undertaken if the lesion had been directly observed and recorded.

3. The good results in 2 seemingly hopeless cases offered a ray of hope in a depressing situation.

4. The presence of immediate complete paralysis did not indicate a hopeless condition.

5. Early surgical intervention gave the patient the best possible chance for recovery of any remaining viable spinal cord.

DISCUSSION

DR. PAUL C. BUCY: Dr. Tinsley has presented this tragic picture well. There is probably no field of neurologic surgery in which the surgeon is rewarded so little for his efforts as here; in 2 cases out of 22 there was definite evidence of improvement. But I should agree entirely with Dr. Tinsley that in these cases of penetrating wounds of the spine with injury to the spinal cord, and usually with foreign bodies present, early operation with débridement and removal of foreign material is the proper treatment. Any other course of treatment will usually lead to serious, often fatal, infection. However, it should be borne in mind that such an operation will do little to benefit the existing injury to the spinal cord, although it may well prevent further damage from infection and from the reaction to the foreign material. In civilian life, penetrating wounds of the spine are unusual, and, accordingly, there are fewer occasions when there is any indication for an open operation in case of injury to the spine and the spinal cord.

DR. HAROLD VORIS: I should like to express my admiration of Dr. Tinsley's courage in operating in these cases, when it is well known how little one usually can expect in the way of neurologic improvement. I have taken foreign bodies out of the spinal cord in a few cases and can recall only 1 instance in which it was worth while; in that case the body was in the region of the cauda equina, where it is known that the outlook for neurologic recovery is more hopeful. A foreign body in the spinal canal presents a definite indication for removal from the standpoint of sepsis, as has been pointed out; but unless there is actual evidence of foreign material in the spinal canal, surgical intervention is not indicated and from the neurologic standpoint the picture is dismal.

In a case recently under my observation in which there was a bullet wound of the cauda equina, with the bullet lodged anterior to the spine, remarkable improvement occurred without surgical intervention. The patient had been in another hospital for two weeks and was in Cook County Hospital for three or four weeks; he has now graduated to a walker. Perhaps some of the patients who have improved after operation might have done so without surgical treatment. However, there is definite indication for débridement of a compound wound or removal of a foreign body from the spinal cord.

DR. MILTON TINSLEY: I tried to stress that these were compound spinal wounds. I know that with civilian injuries of the simple fracture type this operative procedure does not hold. However, even though there is no foreign body in the spinal canal, if there is a compound spinal wound with fracture of the laminas, I believe that laminectomy is indicated, to remove any indriven particles that may not be seen in the roentgenogram.

Cortical Areas of the Albino Rat. Dr. Wendell J. S. Krieg.

The identification and arrangement of the cortical areas of the albino rat were determined on the basis of material stained for cells and myelin, sectioned in various planes, reconstructed into a model and illustrated by comparable strips from sections perpendicular to the surface. About forty cortical areas were distinguished and numbered in an attempt to conform to Brodmann's plan.

It was stated that the parietal cortex has been subdivided in a manner that may be more easily equated with that of higher forms. The auditory cortex (41) has been identified, a finding which changes radically the pattern formerly claimed for the lateral region of lower mammals. In the parietal region, distinct areas 3, 1 and 2 occupy a prominent place, while the associative areas 7 and 39 and the temporal associative area are, as was to be expected, smaller. The primary receptive areas dominate the cerebrum. Motor, premotor and frontal areas are distinguished, the last subdivisable into three areas. The limbic lobe is highly developed and presents numerous structural types.

Study of the myelin pattern in the cortex shows distinctions more striking than those in cellular preparations, and these were utilized in delimitation of areas. In the rat many interareal association fibers are found within the cortex, in its lower layers.

The author stated that identification of cortical areas is contingent on the results of the experimental analysis of their connections now in progress.

DISCUSSION

Dr. Gerhardt von Bonin: I know only the monkey cortex. The connection between area 17 and the retrosplenial area is apparently common to all mammals. I found it in the macaque, in the chimpanzee and in man.

I was interested to see that the motor area in the rat contains a definite inner granular layer. I have committed myself by stating that this layer is present in primates too. The "postcentral" formations have given rise to doubt in my mind. I am not sure about the extent of the somesthetic areas. Does this whole area receive afferent fibers from the ventromedial nucleus of the thalamus? I am impressed with the extent of area 10. I have not had much experience with the dog and cat brain, but my impression is that the frontal sector is even smaller in these forms than in the rat. I wonder whether Dr. Krieg has had any experience with the brains of these carnivores.

The parietal associative areas show a progressive increase in primates. In the macaque there is some differentiation between areas 5 and 7, but areas 39 and 40 are extremely small. Even in the chimpanzee areas 39 and 40, although larger, look similar to each other.

I have studied the macaque and the chimpanzee brains for area 19, and I do not find it. It is impossible to find a clear boundary between area 18 and area 19, despite the fact that some workers have said they could.

Neurologists should be extremely grateful to Dr. Krieg for filling the gap in the knowledge of lower mammals and making it unnecessary to rely on the indirect evidence from the mouse, which I have learned to distrust.

Dr. Percival Bailey: I was much intersted to hear Dr. Krieg say he placed so much reliance on myelin studies. I have had the opposite experience. They are so unreliable that I have discontinued them. The slightest variation in length of differentiation alters the picture of the fibers. Also, one might quarrel with the Brodmann scheme of numeration. He did not publish any description of these areas in the human brain and very little in the animal brain. In the monkey brain, on which he made his chief study, he said himself that a great deal of his work was unreliable and that much of his scheme was gratuitous. So my colleagues and I have given up his scheme in favor of that of von Economo and Koskinas, for they have described in great detail what they mean by their subdivisions of the human cortex. Since our ultimate purpose is to understand the human cerebral cortex, we propose to follow the system of von Economo.

Finally, I should like to express my idea of area 2. After reading the descriptions of Brodmann and all the others, I still do not know what is meant by area 2. I cannot get any mental picture of it. I cannot find any zone of constant structure between area 1 and area 5. I do not believe there is any extra area there. There may be in the human brain, although I cannot get any clear picture of it, but certainly not in the macaque. For some of these areas, therefore, I think that such subdivisions as Dr. Krieg has made must be accepted with reservations, since Brodmann did not say clearly what he meant by them. In spite of the enormous amount of work done on this matter, the subject is still in its infancy. There is plenty of opportunity to make a plan; the important thing is for all to record accurately and definitely what they mean by the different areas they distinguish, so that any one scheme can be checked with others. This was not done by Brodmann, and for that reason I think it inadvisable to continue to use his scheme as though it were a bible.

DR. WENDELL J. S. KRIEG: With respect to area 2 versus area 5, I should be quite willing to accept area 5 in the sense in which it has been defined. It is a parietal area, but it receives the main projection from the ventrolateral region of the thalamus. I want to make it clear that this survey is a preliminary one for my own use, and not primarily for some one in generations to come. The lesions, of which I have about 100, are to be analyzed from the standpoint of these areas. I am quite sure it will be necessary to modify and change my present concept—the lesions are analyzed but not synthesized.

Area 10 is not so large as it appears in the picture; it is small in its medullary aspect. I am not so certain about the partition of the frontal area as I am about other regions.

Dr. Bailey's statement about myelin stains is true; one working on monkey brains would take that attitude. But with the rat brain it is different. There are a tremendous number of fibers within the cortex; and if the myelin picture were left out of consideration, one would lose an important source of understanding. My reason for sticking to Brodmann's system is a concession to a large number of people—clinical workers and students who refer to cortical areas by his numbers. If this system can be kept so far as possible, it will save much confusion. My ultimate purpose is the same as that of the Illinois group, to understand the human brain—the over-all picture—and then gradually to add to the anatomic picture.

Book Reviews

Group Psychotherapy: Theory and Practice. By J. W. Klapman, M.D. Pp. 344, New York: Grune & Stratton, Inc., 1946.

In a field still so fluid and experimental, new books and publications are inevitable. This book has, however, the merit of attempting to lay a theoretic basis for the practice of group psychotherapy, now so popular as a result of military experience. This basis the author finds in the cultural and social heredity of man. He accepts the Cooley-Mead-Dewey-Faris theory of personality, as expressed in Kingsley Davis' dictum that "human nature is determined by the child's communicosocial contacts as much as by his organic equipment." Mental disorder from this standpoint may be described in terms of a breakdown in the regulators of social existence. "To integrate them again with the body of the psyche . . . would seem most feasible in the kind of medium where they had their birth." This leads naturally into a discussion of the problems of group transferences and interactions in relation to the dynamics of therapy.

The author reviews briefly the history of group therapy, from the ancient world of King Saul and Socrates to the modern period of the "scientific and conscious use of the medium of group influence." It is of interest to note that the first modern use of the method was with tuberculous patients by Pratt in 1905. The group method of treatment has since been expanded until now it is in use in a wide variety of diseases, both somatic and psychiatric. With psychiatric disorders group therapy has had an equally wide range of expression, from Schilder's intensive work using psychoanalytic concepts through to the repressive-inspirational technics of Alcoholics Anonymous, Inc.

The actual practice of group therapy is discussed with reference to the outpatient clinic, children's guidance clinics (and the mothers of "problem children"), private practice and the large hospital for patients with mental disease. The obvious factors of saving of time and labor, in addition to the problems of size of the group and selection of cases, and the interrelation of individual and group therapy are fully discussed. The author, who is a member of the faculty of Northwestern University Medical School, gives his own methods in a mental disease hospital setting under the general title of "orientative re-educational psychotherapy." According to him, the relation of the intellect to the affect is "a close and reciprocal one," and intellectualization in his groups is therefore not merely superficial. It is dynamic in itself.

The book is somewhat uneven in style, and some of the material, at least, gives evidence of having actually been used in patient groups for "orientative re-education." A more serious fault is the complete omission of cases having an organic background in his discussion of the role of group therapy in psychiatric cases. The book is of value, however, in its many practical suggestions for the actual practice of the method. As an introduction to the subject of group psychotherapy it may be commended.

Progress in Neurology and Psychiatry: An Annual Review. Edited by E. A. Spiegel, M.D. Price, $8. Pp. 708. New York: Grune & Stratton, Inc., 1946.

With this volume, the editor inaugurates a yearly review of advances in neurology and psychiatry. The usefulness and success of the annual reviews in biochemistry and physiology allow one to predict that a counterpart in neurology and psychiatry will gain rapid acceptance.

With the added impetus of wartime research, the assembling of an exhaustive review can be no simple problem. It is gratifying to report that the task is well

done. A vast amount of useful information is contained in this volume, and, in general, controversial issues are presented with objectivity. The sections on psychiatry are splendidly prepared and should prove of great value to the clinician.

If this reviewer might express a wish it would be that editors always conceive it a duty to be frankly critical. The clinician must be given the chance to judge the basic facts of a new concept of therapy. A case in point is the recent interest in the use of neostigmine as a neuromuscular depressant in cases of poliomyelitis, cerebral palsy, rheumatoid arthritis and conditions of the lower part of the back. The physiologic rationale for this widely popularized form of treatment deserves a great deal of discussion by competent authorities. Yet a puzzled clinician might search in vain for a critical survey of the fundamental issue by a respected, objective editor.

Carping over minor errors in proof is admittedly unbecoming, but attention must be called to a rather serious error in the statement, "quinidine hydrochloride has a considerable beneficial effect [in myasthenia gravis]." Also, in the section on surgery of the spinal cord, Scott discusses a case of reverse spondylolisthesis. He describes a patient with complete bilateral spastic paraplegia. This surprising statement then follows: "Laminectomy was considered but not done because the child was able to walk following straightening of the knees and elongation of the Achilles tendon."

Since this volume fills a major need and maintains laudable editorial standards, it is recommended to the student of the fields.

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